CHAPTER 10

NEOPLASIA ASSESSMENT

INTRODUCTION

Background

Despite conclusive evidence that chlorophenols are potent carcinogens in laboratory animals, the carcinogenicity of dioxin in humans remains controversial. Traditional difficulties in extrapolating animal data to humans have limited the applicability and relevance of much of the experimental work.

Numerous long-term exposure studies have established the carcinogenicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD, or dioxin) in rats (1,2), mice (3-5), and hamsters (6). The consensus of most research is that TCDD is only weakly mutagenic and does not covalently bind to DNA or cause it to initiate repair synthesis, but that it does behave as a strong tumor promoter at the cellular level (7).

The oncogenic response to TCDD in animals has been shown repeatedly to depend upon the age, sex, and strain of species as well as the dose and route of administration (8-10). In varying doses and routes of administration, TCDD has produced malignant neoplasms at multiple sites in rats (lung, oropharyngeal, thyroid, adrenal, and liver) (2,3), in mice (thyroid, thymus, connective tissue, and liver) (3), and in hamsters (cutaneous) (6). As summarized in detail in a recent review article (11), much of the basic research into the carcinogenicity of TCDD in laboratory animals has focused on the aryl hydrocarbon (Ah) receptor and the induction of the cytochrome P-450 enzyme system (12-16). Though the Ah receptor has been isolated from the tissue of several human organs (e.g., liver, colon, tonsils) (17-22), the relevance of these observations to dioxin toxicity remains to be proven (23).

Most of the longitudinal epidemiologic studies of TCDD toxicity in humans have included malignancy as a principal clinical endpoint and have been based on cohorts of veterans who served in the Vietnam era (24-28) and of civilian populations exposed to dioxin by occupation (29-37) or as a consequence of industrial accidents (38-42). The literature based on research prior to 1987 has been summarized in earlier reports of the Air Force Health Study (AFHS) (25,43) and will not be reviewed in detail. Two more recent large-scale studies, though not designed to correlate clinical endpoints with exposure to Herbicide Orange, have focused on the incidence of specific cancers in Vietnam veterans.

The Department of Veterans Affairs is conducting a proportionate mortality study of Army and Marine Corps veterans of the Vietnam era. The study has now been expanded to include 62,068 veterans who died between 1965 and 1984. The finding in an earlier report (44) of an increased incidence of lung cancer and non-Hodgkin's lymphoma in Marine Vietnam veterans was not confirmed in a more recent study of similar design in U.S. Army veterans who served in the same region at the same time (45). In another report (46), Army

veterans were found to have an increased mortality from cancer of the lung and larynx. The Vietnam Experience Study (VES) and the Selected Cancers Cooperative Study Group conducted by the Centers for Disease Control (CDC) have defined an increased risk for the development of non-Hodgkin's lymphoma associated with military service in Vietnam but no relationship to potential exposure to Herbicide Orange (47,48). These results conflicted with the findings from another Veterans' Administration hospital-based study (49) and other reports from the VES have found no increase in the incidence of Hodgkin's disease (50) or soft-tissue and other sarcomas (51).

The development of assay techniques that permit the accurate determination of the current body burden of dioxin has placed the current investigation on a much more scientific footing. As the only study of military veterans incorporating serum dioxin levels into data analysis, the AFHS is unique among those studies addressing the history of malignancy in those who served in the Vietnam War (24). Stratification of the Ranch Hand cohort by occupation revealed significantly higher mean levels of serum dioxin in the enlisted groundcrew (23.6 parts per trillion [ppt]) and the enlisted flyers (17.2 ppt) than in the officers (range of 6.7 - 9.3 ppt).

There was no significant difference between the cohorts in the overall history of malignancy. Though there is no evidence that TCDD exposure causes skin cancer in humans, the Baseline and subsequent followup examinations found an increased history of basal cell carcinoma in the Ranch Hand cohort versus the Comparison cohort. Stratified analysis based on serum dioxin levels, however, did not reveal a dose-response effect. The greatest number of these skin cancers occurred in those participants (officers) with the lowest mean serum dioxin levels. In a pattern consistent with a dose-response effect, the history of benign systemic neoplasms was greater in Ranch Hands than in Comparisons, most of these neoplasms were lipomas. With reference to those systemic cancers that have been suspect as related to TCDD exposure, there has been one case of soft tissue sarcoma (STS) in each cohort (Ranch Hand and Comparisons) and one case of Hodgkin's disease in a Ranch Hand participant.

Apart from the AFHS, several published reports have incorporated tissue levels of TCDD into the analysis of data derived from populations exposed by occupation (14,29,52) or by industrial accidents (39,40,53). As part of the National Institute of Occupational Safety and Health's (NIOSH) Dioxin Registry, one study examined cause-specific mortality among 5,172 workers exposed to TCDD at 12 chemical production plants (29). Exposure was documented by job description and by correlation with serum TCDD levels in 253 workers in the surviving cohort. The median serum TCDD level in living members of the exposed cohort was 233 parts per trillion and 7 ppt in the unexposed cohort. In exposed workers, there was a slight but statistically significant increase in mortality from all cancers combined but not from those malignancies putatively associated with TCDD exposure (non-Hodgkin's lymphoma, Hodgkin's disease, and STS). In a subcohort of 1,520 workers with a longer period of exposure (more than 1 year; mean serum TCDD of 418 ppt in 119 samples) and greater latency (more than 20 years since first exposure) there was a further increase in mortality from all cancers combined and a significantly increased mortality from soft-tissue sarcoma and for cancers of the respiratory tract.

Though the authors of the NIOSH study recognized such methodologic limitations as low statistical power, misclassification of death certificates, and potential confounders, some of their results were similar to those reported in the most recent study of German chemical workers exposed to TCDD during and after a chlorophenol reactor accident in 1953 (40). Within the total study group of 247, a subcohort of 69 was defined. All of these men developed chloracne and, for those tested, the median serum TCDD level was 24.5 ppt. In this most heavily exposed group, there was a statistically significant increase in mortality from all cancers combined although, as in the NIOSH study, the effect was apparent only in those with latency greater than 20 years. A similar latency effect was noted in another mortality study of 1,583 workers employed at the same plant (after the explosion) from 1954 to 1984 (33). Participants were stratified into high and low exposure groups by job classification and, in 48 individuals, by adipose tissue levels of TCDD (average of 296 ng/kg and 83 ng/kg respectively). In the highly exposed group, standardized mortality ratios (SMRs) for all causes of death were elevated relative to two comparison cohorts and the risk became clearly more pronounced in those with more than 20 years employment (SMRs rising from 1.24 to 1.87 and 1.39 to 1.82 versus the two comparison cohorts). Potential limitations of this study were acknowledged and commented upon separately (54).

Finally, the limited amount of tissue level data that has become available from the 1976 industrial explosion at Seveso, Italy reflects the extreme level of exposure that occurred. In the area closest to the source (Zone A), serum levels of TCDD ranged from 828 ppt to 56,000 ppt, the highest ever recorded in humans (53). Cancer surveillance has been limited by the small number of cases observed. In the most recent report that covers the decade up to 1986 (39), slight increases in the risk of several malignancies have been noted but, with the exception of the occurrence of biliary cancer in women, were not statistically significant.

Summary of Previous Analyses of the Air Force Health Study

1982 Baseline Study Summary Results

Cancer received major emphasis during the AFHS Baseline examination in 1982. The neoplasia assessment used data from both the in-home questionnaire and the review-of-systems questionnaire obtained during the physical examination as well as data from the examination itself. All subjective data were verified by medical record reviews. In addition, tabulation of mortality count data from the Baseline Mortality Report was used in conjunction with cancer morbidity information. The overall results did not show a significant difference in systemic cancer between the two groups but did show significantly more skin cancer ($p=0.03$) in the Ranch Hand group.

Of 50 reported systemic cancers from the Ranch Hand and Comparison groups, 28 (14 in each group) were verified by medical records and pathology reports. A visual inspection of anatomic sites showed a slight excess of genitourinary cancer and oropharyngeal cancer but a relative deficit of digestive system neoplasms in Ranch Hands. A combined morbidity-mortality assessment derived from the initial 1:1 match (Ranch Hand to the Original Comparison member) disclosed similar distributions. One case of STS and one case of Hodgkin's disease were confirmed, both in the Comparison group. Exposure analyses for industrial chemicals and x rays were negative.

Questionnaire data verified by medical record reviews revealed significantly more skin cancer in Ranch Hands (odds ratio 2.35). Basal cell carcinoma accounted for 83.9 percent of the reported skin cancers in both groups and was concentrated anatomically on the face, head, and neck. The few melanoma and squamous cell cancers were distributed evenly between the Ranch Hand and Comparison groups. Adjustments for occupational exposures (e.g., asbestos, degreasing chemicals) did not alter the increased rate of skin cancer in the Ranch Hand group. Skin cancer in both groups was associated with exposure to industrial chemicals ($p=0.03$). Outdoor occupations subsequent to military service as a covariate did not account for the significant skin cancer association.

1985 Followup Study Summary Results

The Baseline and 1985 followup data were combined for the assessment of lifetime history of cancer; occurrences of cancer prior to their service in Southeast Asia (SEA) were excluded.

For the unadjusted analyses (Blacks and non-Blacks included), Ranch Hands had a significantly greater frequency of a verified skin neoplasm (malignant, benign, or uncertain behavior or unspecified nature) than Comparisons. There were no significant unadjusted group differences among non-Black participants for basal cell carcinoma, squamous cell carcinoma, melanoma, or all malignant skin neoplasms. For verified sun exposure-related malignant skin neoplasms, Ranch Hands had a marginally significantly greater frequency than Comparisons. The groups did not differ significantly for verified and suspected sun exposure-related malignant skin neoplasms. The adjusted group contrast in histories of the sun exposure-related skin cancers, the majority of which were basal cell carcinomas, also was significant ($p=0.030$).

The unadjusted group contrasts of the incidence rates of all systemic cancers combined were not significant. There was one new occurrence of an STS (Ranch Hand) and one suspected cancer of the lymphatic system (Ranch Hand), in addition to the one previously reported STS and one Hodgkin's disease in the Comparison group. There were no cases of non-Hodgkin's lymphoma in either group at the time of the 1985 report.

1987 Followup Study Summary Results

The unadjusted analysis of all verified neoplasms indicated that the proportion of Ranch Hands with a neoplasm was significantly greater than that of Comparisons. After including suspected neoplasms with verified neoplasms, the Ranch Hand proportion was marginally greater than the Comparison proportion. The majority of malignant neoplasms observed in Ranch Hands were basal cell carcinomas, a nonlife-threatening form of skin cancer. When the analysis was performed only on skin neoplasms for non-Black participants, significantly more Ranch Hands had a skin neoplasm than did Comparisons.

In the unadjusted analyses of verified basal cell carcinoma, a marginally significant group difference was found. After adjustment for covariates, the group contrast was statistically significant for verified basal cell carcinoma. Also, Ranch Hands had a

significantly higher percentage of participants with multiple verified basal cell carcinomas than did Comparisons.

Sun exposure-related malignant skin neoplasms also exhibited group differences. (Approximately 90 percent of the participants with a sun exposure-related malignant neoplasm had a basal cell carcinoma.) For the unadjusted analysis, the group contrast was significant for verified diagnoses. For the adjusted analysis of these neoplasms, Ranch Hands and Comparisons differed significantly.

No significant group differences were found in the analyses of systemic neoplasms by number, behavior (malignant, benign, or uncertain behavior or unspecified nature), or location and site. Thus, the increase in overall malignancy was due to elevated relative risks for skin cancer (basal cell carcinoma). The number of STS and non-Hodgkin's lymphoma was comparable in the two groups.

Serum Dioxin Analysis of 1987 Followup Study Summary Results

The analyses generally did not establish a significant positive association between dioxin and the presence of a skin neoplasm. Significant relative risks were found for the skin neoplasm analyses; however, the relative risks were almost always less than 1. For the analyses focusing on enlisted flyers with a basal cell carcinoma of other sites (and a sun exposure-related malignant skin neoplasm of other sites), relative risks were found to be significant and greater than 1. However, these results may be the consequence of a multiple-testing artifact, since they were not noted for the enlisted groundcrew who, as a group, had higher levels of serum dioxin than the enlisted flyers.

In general, the analyses of all systemic neoplasms combined produced some significant or marginally significant relative risks greater than 1. The relative risk for participants with a benign systemic neoplasm (such as a lipoma) was significantly greater than 1, in contrast to nonsignificant relative risks, which were often less than 1, for participants with a malignant systemic neoplasm.

The study provides no evidence of increased incidence for the neoplasms most commonly suspected as being associated with exposure to chlorophenols (Hodgkin's disease, non-Hodgkin's lymphoma, and STS). However, the number of participants with these specific neoplasms was small; therefore, the statistical power to detect small or moderately elevated relative risks was low. There is no evidence of a relationship between dioxin and either skin or systemic cancer in these data. There is a suggestion of a dose-related relationship between dioxin and benign systemic neoplasms (lipomas) that was explored in greater depth in the 1992 physical examination.

Parameters for the Neoplasia Assessment

Dependent Variables

The neoplasia assessment was based on the occurrence of neoplasms after service in SEA. Information on the occurrence of neoplasms was captured in the health questionnaires

and the physical examinations at Baseline (1982) and at the 1985 followup and 1987 followup studies and was coded according to conventions in the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) manual. This information was combined with data collected at the 1992 followup to form a complete neoplastic history for each participant.

The term "neoplasm" refers to any new growth that may or may not be malignant. Malignant neoplasms are those neoplasms capable of invasion and metastasis. Malignant and benign neoplasms, carcinomas in situ, and neoplasms of uncertain behavior or unspecified nature as well as skin and systemic neoplasms were studied. "Systemic neoplasm" denotes a nonskin neoplasm.

The neoplasia assessment was based on the number of participants with a neoplasm, and not on the number of neoplasms. A participant was considered to have an adverse health condition for the neoplasia assessment if he had one or more neoplasms.

Verified Medical Records Data

During the 1992 health interview, each study participant was asked a series of questions on the occurrence of cancer since the date of his last health interview. The self-reported conditions were verified by medical record review. Only data on verified neoplasms were used in the neoplasia assessment.

Some possible neoplastic conditions were discovered by the physicians at the physical examination. Contingent upon participant authorization, suspicious skin lesions were biopsied, and the pathology determined; however, no other invasive procedures were used to detect systemic neoplasms.

Skin Neoplasms—The analysis of skin neoplasms for the neoplasia assessment was divided into two sets. Analysis Set 1 consisted of analyses of skin neoplasms by behavior type. Four behavior types were examined: (1) all skin neoplasms, (2) malignant skin neoplasms only, (3) benign skin neoplasms only, and (4) skin neoplasms of uncertain behavior or unspecified nature.

Analysis Set 2 consisted of analyses of malignant skin neoplasms by cell type. The following four cell types were analyzed: (1) basal cell carcinomas, (2) squamous cell carcinomas, (3) nonmelanoma (basal cell carcinomas, squamous cell carcinomas, and malignant epithelial neoplasms not otherwise specified), and (4) melanoma. Analyses of basal cell carcinomas were conducted for all sites combined and by location or site. The following four locations or sites were examined for basal cell carcinomas: (1) ear, face, head, and neck; (2) trunk; (3) upper extremities; and (4) lower extremities. There were no basal cell carcinomas on other sites or sites not otherwise specified.

There are relatively few Black participants in this study (approximately 5%), and they have been observed only to exhibit benign skin neoplasms in all phases of the study to date. Consequently, skin neoplasm analyses, except for the analyses of benign skin neoplasms, were limited to non-Blacks. Both Blacks and non-Blacks were included in the analysis of

benign skin neoplasms. Participants with a pre-SEA skin neoplasm were excluded from the analysis of the skin neoplasm variables to avoid any bias caused by predisposition to malignancy.

Systemic Neoplasms—The systemic neoplasms were analyzed by behavior and body site. As with skin neoplasms, each analysis was conducted using verified data. The analysis of the systemic neoplasms was divided into two sets, described below.

Analysis Set 1 consisted of analyses of systemic neoplasms by behavior type. The following four behavior types were examined: (1) all systemic neoplasms, (2) malignant systemic neoplasms, (3) benign systemic neoplasms, and (4) systemic neoplasms of uncertain behavior or unspecified nature.

Analysis Set 2 consisted of analyses of malignant systemic neoplasms by the following sites: (1) eye, ear, head, face, and neck; (2) oral cavity, pharynx, and larynx; (3) esophagus; (4) brain; (5) thymus and mediastinum; (6) thyroid gland; (7) bronchus and lung; (8) colon and rectum; (9) kidney and bladder; (10) prostate; (11) testicles; (12) ill-defined sites; (13) connective and other soft tissues; and (14) carcinomas in situ of the penis and of other and unspecified sites.

In addition to the analyses described above, the number of participants with Hodgkin's disease, leukemia, non-Hodgkin's lymphoma, a malignant systemic neoplasm of lymphoid and histiocytic tissue, and multiple myeloma were analyzed.

Participants with a pre-SEA malignant systemic neoplasm or a pre-SEA systemic neoplasm of uncertain behavior or an unspecified nature were excluded from the analysis of the systemic neoplasm variables.

Skin and Systemic Neoplasms—All neoplasms, skin and systemic combined, were analyzed. Participants with a pre-SEA skin neoplasm and participants with a pre-SEA malignant systemic neoplasm or a pre-SEA systemic neoplasm of uncertain behavior or an unspecified nature were excluded from the analysis of this variable.

Laboratory Examination Data

The prostate-specific antigen (PSA) test is relatively new and was developed to detect prostate enlargement and prostate cancer. Each participant had his PSA measured as a standard portion of the laboratory assay. This measurement is continuous in nature, and the units are ng/ml. Analysis was performed on the continuous measurement, as well as on a discrete form, which is categorized as "normal" or "abnormal," with a cutpoint of 4 ng/ml.

Covariates

The emphasis on choosing risk factors related to cancer was increased during the 1985 followup study and has been emphasized since that time. In particular, the interval health questionnaire was modified to collect information on each geographic location in which a participant lived for more than 12 months. Because ultraviolet light exposure has been

acknowledged as the primary cause of basal cell carcinomas, this information was used to compute a cumulative sun-exposure index based on residential history. An average lifetime residential latitude was estimated by dividing the total degree-years (i.e., the sum of the product of latitude [degrees] and the number of years lived at each residence) from all residences by the total number of residential years reported on the questionnaire.

The denominator of the average lifetime residential latitude covariate is based on the total number of years at each residence. Because this information is reported by the participant, it is subject to under- or over-reporting. For each of the 2,219 participants who provided information on their residential history, the following ratio was constructed:

$$\frac{\text{years reported - age in years}}{\text{age in years}}$$

This ratio was greater than 0.35 for three participants (over-reporting of their residences) and less than -0.35 for six participants (under-reporting of their residences). The average lifetime residential latitude covariate is available for 2,210 participants. This covariate was then dichotomized as less than 37 degrees latitude or greater than or equal to 37 degrees latitude, the approximate median of the covariate.

In the analysis of the 1992 examination results, candidate covariates in adjusted statistical analyses assessing skin neoplasms included age, skin color, hair color, eye color, reaction of skin to sun exposure after at least 2 hours, reaction of skin to sun exposure after repeated exposure, average lifetime residential latitude, and lifetime exposure to asbestos, ionizing radiation, industrial chemicals, herbicides, insecticides, and degreasing chemicals. Information on eye, skin, and hair color was obtained for participants who did not attend either the 1985 or 1987 examinations. The participants' lifetime exposure to the six carcinogens described above was updated. Additionally, race was a used as a candidate covariate for the analysis of benign skin neoplasms. A composite sun-reaction index, which is a composite of the two individual reactions of skin to sun covariates, was used in previous cycles of the AFHS. The two individual reaction of skin to sun exposure variables were used instead of the composite variable because the composite variable was highly correlated with the two individual covariates and the individual covariates were more useful in explaining the skin neoplasia dependent variables. Also, the composite sun-reaction index was highly correlated with the two individual reaction of skin to sun covariates, thereby complicating analyses. The relationship between the skin neoplasm dependent variables and the composite sun-reaction index is shown in Appendix Table F-1-1 to illustrate the similarities of this covariate to the two individual sun-reaction covariates; however, this covariate is not used in the adjusted analysis.

The lifetime alcohol history covariate was based on self-reported information from the 1992 questionnaire and combined with similar information gathered at the 1987 followup. The respondent's average daily alcohol consumption was determined for various drinking stages throughout his lifetime, and an estimate of the corresponding total number of drink-years (1 drink-year is the equivalent of drinking 1.5 ounces of 80-proof alcoholic

beverage per day for 1 year) was derived. For lifetime cigarette smoking history, the respondent's average smoking was estimated over his lifetime based on his responses to the 1992 questionnaire, assuming 365 packs of cigarettes equal 1 pack-year.

Similar to the analysis of all other clinical areas, occupation was included in analyses of Model 1 (see Chapter 7, Statistical Methods, for a description of the basic statistical analysis approaches used). In general, enlisted personnel had higher levels of exposure than officers, with enlisted groundcrew having higher levels than enlisted flyers. Occupation was not considered to be a risk factor in the neoplasia assessment, however, and was not used in adjusted analyses of Models 2 through 6.

Herbicide exposure was included as a candidate covariate in the statistical analysis. Exposure to herbicides naturally has a high association with group (Ranch Hand, Comparison), and it is recognized that adjusting for herbicide exposure has the potential to over-adjust for the effects of dioxin exposure. The intent of the question was to capture information on post-SEA exposure. As seen by the frequencies for this covariate in Chapter 8, Covariate Exposures with Measures of Dioxin Exposure, it appears as if both Ranch Hands and Comparisons misinterpreted this question to apply to SEA experiences as well.

The potential for over-adjusting is most likely for the two models that use Comparisons (Models 1 and 3). As seen in Chapter 8, herbicide exposure is highly associated with group status in the two models using Comparisons (Models 1 and 3). The other models do not show a relationship between dioxin and herbicide exposure in the Ranch Hand cohort (Models 2, 4, 5, and 6). To investigate the effects of adjustment for herbicide exposure, analyses were performed with and without herbicide exposure in the final model when the final adjusted model contained this covariate. Analyses without herbicide exposure in the final model showed no difference from the results described subsequently in the text.

Categories of candidate covariates and definitions are provided below:

- Skin Color: dark, medium, pale, dark peach, and pale peach. (Classified for analysis purposes as (1) dark, medium, pale, or (2) dark peach, pale peach.)

- Hair Color: black, dark brown, light brown, blonde, red, and bald. (Classified for analysis purposes as (1) black, dark brown, or (2) light brown, blonde, red, bald.)

- Eye Color: brown, hazel, green, gray, and blue. (Classified for analysis purposes as (1) brown, (2) hazel, green, or (3) gray, blue.)

- Reaction of Skin to Sun Exposure After at Least 2 Hours, After First Exposure: burns painfully, burns, becomes red, and no reaction.

- Reaction of Skin After Repeated Exposure: freckles with no tan, tans mildly, tans moderately, and tans deep brown.

- Composite Sun-Reaction Index (not used in adjusted exposure analysis): a composite variable based on two reaction of skin to sun exposure variables was defined as

follows: (1) burns painfully or freckles with no tan, (2) burns or tans mildly, and (3) all other reactions.

- Average Lifetime Residential Latitude: average latitude less than 37° and average greater than or equal to 37°.

- Exposure to Carcinogens: asbestos, ionizing radiation, industrial chemicals, herbicides, insecticides, and degreasing chemicals (yes or no for each). These exposures represent lifetime exposure based on self-reported questionnaire data from this examination combined with previous examinations.

The candidate covariates for the systemic neoplasia assessment and the analysis of PSA was the same as those for the skin neoplasia assessment with the following exceptions:

- Race was added as a candidate covariate for all systemic neoplasm analyses.

- The following covariates specific to skin were deleted: skin color, hair color, eye color, reactions of skin to sun exposure, and average lifetime residential latitude.

Statistical Methods

Chapter 7, Statistical Methods, describes the basic statistical analysis methods used in the neoplasia assessment. Table 10-1 summarizes the statistical analyses that were performed for the neoplasia assessment. The first part of this table identifies the dependent variables and the statistical methods. This information is presented in the following three sections: skin neoplasms, systemic neoplasms, and skin and systemic neoplasms. Data source, data form, cutpoints, and candidate covariates are summarized at the end of the table. The second part of the table describes the candidate covariates. Abbreviations used in the body of the table are defined at the end of the table. Table 10-2 provides the number of participants with missing dependent variable data and those excluded due to a history of a pre-SEA neoplasm.

The Neoplasia Assessment contains many covariates for use in adjusted analyses of skin and systemic neoplasms. Additionally, less than one percent of the participants have a history of a neoplasm for over half of the dependent variables. Consequently, the attempts of the modeling strategy for this clinical area were to include as many covariates as main effects and group-by-covariate interactions as feasible (covariate-by-covariate not explored). When the number of participants with a history of a particular neoplasm was too small to support analysis of interactions, models including only the candidate covariates as main effects were investigated. If the number history of participants with a particular neoplasm was still too small to support meaningful analysis, only the continuous covariates of age, lifetime cigarette smoking history, and lifetime alcohol history were included as candidates for the final adjusted model. Other endpoints had so few participants that adjusted analysis was not possible; only unadjusted analyses are specified for these variables and are noted in Table 10-1.

Table 10-1.
Statistical Analyses for the Neoplasia Assessment

Dependent Variables

Category	Location or Site	Statistical Analyses
	Skin Neoplasms	
Behavior		
All	All Sites Combined	U:LR,CS A:LR
Malignant	All Sites Combined	U:LR,CS A:LR L:LR
Benign	All Sites Combined	U:LR,CS A:LR
Uncertain Behavior or Unspecified Nature	All Sites Combined	U:LR,CS A:LR
Cell Type and Location or Site		
Basal Cell Carcinoma	All Sites Combined Ear, Face, Head, and Neck Trunk Upper Extremities Lower Extremities	U:LR,CS A:LR
Squamous Cell Carcinoma	All Sites Combined	U:LR,CS A:LR
Nonmelanoma	All Sites Combined	U:LR,CS A:LR
Melanoma	All Sites Combined	U:LR,CS A:LR
	Systemic Neoplasms	
Behavior		
All	All Sites Combined	U:LR,CS A:LR
Malignant	All Sites Combined	U:LR,CS A:LR L:LR
Benign	All Sites Combined	U:LR,CS A:LR L:LR
Uncertain Behavior or Unspecified Nature	All Sites Combined	U:LR,CS A:LR
Location or Site		
Malignant	Eye, Ear, Face, Head, and Neck	U:LR,CS A:LR
Malignant	Oral Cavity, Pharynx, and Larynx	U:LR,CS A:LR
Malignant	Esophagus	Frequencies
Malignant	Brain	U:LR,CS

Table 10-1. (Continued)
Statistical Analyses for the Neoplasia Assessment

Dependent Variables

Category	Location or Site	Statistical Analyses
Malignant	Thymus, Heart, and Mediastinum	U:LR,CS A:LR
Malignant	Thyroid Gland	U:LR,CS A:LR
Malignant	Bronchus and Lung	U:LR,CS A:LR
Malignant	Colon and Rectum	U:LR,CS A:LR
Malignant	Kidney and Bladder	U:LR,CS A:LR
Malignant	Prostate	U:LR,CS A:LR
Malignant	Testicles	U:LR,CS A:LR
Malignant	Ill-Defined Sites	U:LR,CS A:LR
Malignant	Connective and Other Soft Tissues	Frequencies
Carcinoma In Situ	Penis, Other, and Unspecified Sites	U:LR,CS
Hodgkin's Disease	--	U:LR,CS A:LR
Leukemia	--	U:LR,CS
Non-Hodgkin's Lymphoma	--	U:LR,CS A:LR
Other Malignant Systemic Neoplasms of Lymphoid and Histiocytic Tissue	--	U:LR,CS A:LR
Multiple Myeloma	--	U:LR,CS
	Skin and Systemic Neoplasms	
All	All Sites Combined	U:LR,CS A:LR

Laboratory Variable

Variable (Units)	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Prostate-Specific Antigen (ng/ml)	D/C	Abnormal: >4 Normal: ≤4	AGE,RACE,OCC, PACKYR,DRKYR, ASB,IONRAD,IC, HERB,INS,DC	U:LR,CS,GLM,TT A:LR,GLM

Table 10-1. (Continued)
Statistical Analyses for the Neoplasia Assessment

Covariates

Variable (Abbreviation)	Data Source	Data Form	Cutpoints
Age (AGE)	MIL	D/C	Born ≥1942 Born <1942
Race (RACE)	MIL	D	Black Non-Black
Occupation (OCC)	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Lifetime Cigarette Smoking History (PACKYR) (pack-years)	Q-SR	D/C	0 >0-10 >10
Lifetime Alcohol History (DRKYR) (drink-years)	Q-SR	D/C	0 >0-40 >40
Skin Color (SKIN)	PE	D	Non-Peach: Dark, Medium, Pale Peach: Dark Peach, Pale Peach
Hair Color (HAIR)	PE	D	Black, Dark Brown Light Brown, Blonde, Red, Bald
Eye Color (EYE)	PE	D	Brown, Hazel, Green Gray, Blue
Reaction of Skin to Sun after at Least 2 Hours, after First Exposure (SUN2HR)	Q-SR	D	Burns Painfully Burns Becomes Red No Reaction
Reaction of Skin to Sun after Repeated Exposure (SUNRPT)	Q-SR	D	Freckles with No Tan Tans Mildly Tans Moderately Tans Deep Brown
Composite Sun-Reaction Index (SUNREAC)	Q-SR	D	Burns Painfully (for SUN2HR) or Freckles with No Tan (for SUNRPT) Burns (for SUN2HR) or Tans Mildly (for SUNRPT) All Other Reactions
Average Lifetime Residential Latitude (LAT)	Q-SR	D	Latitude <37° Latitude ≥37°
Asbestos Exposure (ASB)	Q-SR	D	Yes No

Table 10-1. (Continued)
Statistical Analyses for the Neoplasia Assessment

Covariates

Variable (Abbreviation)	Data Source	Data Form	Cutpoints
Ionizing Radiation Exposure (IONRAD)	Q-SR	D	Yes No
Industrial Chemical Exposure (IC)	Q-SR	D	Yes No
Herbicide Exposure (HERB)	Q-SR	D	Yes No
Insecticide Exposure (INS)	Q-SR	D	Yes No
Degreasing Chemical Exposure (DC)	Q-SR	D	Yes No

Dependent Variables (Except for Prostate-Specific Antigen)

Data Source: Review of medical records and verification based on AFHS questionnaires and physical examinations.

Data Form: Discrete.

Cutpoints: Yes or No.

Candidate Covariates for Skin Neoplasms: All covariates listed above except race, lifetime cigarette smoking history, and lifetime alcohol history.

Candidate Covariates for Systemic Neoplasms: All covariates listed above except skin color, hair color, eye color, reaction of skin to sun exposure variables, composite sun-reaction index, and average lifetime residential latitude.

Abbreviations

Data Source:
- MIL = Air Force military records
- PE = Physical examinations
- Q-SR = Health questionnaires (self-reported)

Data Form:
- D = Discrete analysis only
- D/C = Discrete and continuous analyses for dependent variables; appropriate form for analysis (either discrete or continuous) for covariates

Statistical Analyses:
- U = Unadjusted analyses
- A = Adjusted analyses
- L = Longitudinal analyses

Statistical Methods:
- CS = Chi-square contingency table analysis (continuity-adjusted for 2x2 tables)
- GLM = General linear models analysis
- LR = Logistic regression analysis
- TT = Two-sample t-test

Table 10-2.
Number of Participants with Missing Data for, or Excluded from, the Neoplasia Assessment

Variable	Variable Use	Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
		Ranch Hand	Comparison	Initial	Current	Ranch Hand	Comparison
Prostate-Specific Antigen	DEP	0	1	0	0	0	0
Lifetime Cigarette Smoking History	COV	1	2	0	1	1	2
Lifetime Alcohol History	COV	22	21	13	20	20	18
Skin Color*	COV	1	4	0	1	1	0
Hair Color*	COV	0	4	0	0	0	0
Eye Color*	COV	0	6	0	0	0	2
Reaction of Skin to Sun After at Least 2 Hours*	COV	1	3	1	1	1	3
Reaction of Skin to Sun After Repeated Exposure*	COV	4	7	3	4	4	6
Composite Sun-Reaction Index*	COV	1	2	1	1	1	2
Average Lifetime Residential Latitude*	COV	3	19	2	3	3	11
Pre-SEA Skin Neoplasms	EXC	10	9	7	10	10	7
Pre-SEA Malignant Systemic Neoplasms	EXC	5	0	4	5	5	0
Pre-SEA Systemic Neoplasms of Uncertain Behavior or Unspecified Nature	EXC	4	1	2	3	3	1
Black Participants	EXC	56	75	36	51	51	55

*Number of participants with missing data for Non-Black participants only.

Abbreviations: DEP = Dependent variable (missing data).
COV = Covariate (missing data).
EXC = Exclusion.

Note: 952 Ranch Hands and 1,281 Comparisons;
520 Ranch Hands for initial dioxin; 894 Ranch Hands for current dioxin;
894 Ranch Hands and 1,063 Comparisons for categorized dioxin.
One Ranch Hand missing total lipids for current dioxin.

Longitudinal Analysis

Longitudinal analyses of malignant skin neoplasms, malignant systemic neoplasms, and benign systemic neoplasms were conducted to evaluate the association between exposure and the changes in neoplasm status between the 1982 Baseline examination and the 1992 followup examination. See Chapter 7, Statistical Methods, for a further discussion of the methods used in the longitudinal analysis.

RESULTS

Dependent Variable-Covariate Associations

Results from the tests of association between the neoplasia dependent variables and candidate covariates in the combined Ranch Hand and Comparison cohorts are presented in Appendix Table F-1-1.

A history of a skin neoplasm was significantly associated with age, indicating older participants were more likely to have had a skin neoplasm than younger participants ($p<0.001$). Occupation also was significant ($p=0.005$). The percentage of participants having a history of a skin neoplasm increased from enlisted groundcrew to enlisted flyer and then to officers. Participants with skin color categorized as peach were significantly more likely to have had a skin neoplasm than those with non-peach skin color ($p=0.011$). Both skin reaction to sun variables, after at least 2 hours and after repeated exposure, were significantly associated with a history of a skin neoplasm ($p<0.001$ and $p=0.017$ respectively). A history of a skin neoplasm increased as burning or freckling tendencies among participants increased.

Covariates displaying a significant association with a history of a malignant skin neoplasm were age ($p<0.001$), occupation ($p<0.001$), skin color ($p=0.050$), reaction of skin to sun after at least 2 hours exposure ($p<0.001$), and skin reaction to sun after repeated exposure ($p<0.001$). Also significant were the composite sun reaction index, which was directly associated ($p<0.001$), and average lifetime residential latitude ($p=0.001$), which indicated participants who were closer to the equator had more histories of a malignant skin neoplasm.

All tests of association involving benign skin neoplasms were nonsignificant ($p>0.15$ for all covariates). Results were similar for skin neoplasms of uncertain behavior or unspecified nature, except for a significant association with reaction of skin to sun after repeated exposure ($p=0.006$). The freckles with no tan category showed the highest percentage of participants with a history of a skin neoplasm of uncertain behavior or unspecified nature.

A history of a basal cell carcinoma was significant and was directly associated with age ($p<0.001$), occupational rank ($p<0.001$; officers were more likely to exhibit a history of a basal cell carcinoma), potential of skin to burn after initial 2-hour sun exposure ($p<0.001$), potential to freckle or not tan after repeated sun exposure ($p<0.001$), and the composite sun reaction index ($p<0.001$). Also as expected, participants living in more southerly latitudes

had a greater history of a basal cell carcinoma than participants living in more northerly latitudes ($p < 0.001$).

Covariates that were significantly associated with any basal cell carcinoma were similarly associated with a basal cell carcinoma of the eye, ear, face, head, or neck ($p \leq 0.001$ for age, occupation, initial reaction of skin to sun after at least 2 hours, reaction of skin to sun after repeated exposure, composite sun-reaction index, and average lifetime residential latitude). Hair color also displayed a significant association ($p=0.008$). Participants with lighter hair colors had more basal cell carcinomas of the eye, ear, face, head, or neck.

A basal cell carcinoma of the trunk also was associated with age ($p=0.007$), occupation ($p < 0.001$), initial reaction of skin to sun after at least 2 hours ($p=0.002$), reaction of skin to sun after repeated exposure ($p=0.004$), composite sun-reaction index ($p=0.018$), and average lifetime residential latitude ($p=0.019$). A significant negative association with asbestos exposure also was found ($p=0.034$), with more basal cell carcinomas of the trunk among participants with no exposure to asbestos.

Tests of association between covariates and a basal cell carcinoma of the upper extremities revealed significantly more disease among older participants ($p=0.006$), officers ($p=0.001$), those who freckle without tanning after repeated sun exposure ($p=0.011$), and participants with the highest composite sun reaction index ($p=0.049$).

The basal cell carcinoma of the lower extremities variable did not exhibit significant associations with any of the covariates tested ($p > 0.15$ for all tests). Each covariate association test also was nonsignificant or only marginally significant for the squamous cell carcinoma variable ($p > 0.06$ for all tests).

Similar to basal cell carcinoma, nonmelanoma displayed significant associations with several covariates. The age association revealed older participants had a greater history of a nonmelanoma ($p < 0.001$). The test for occupation also was significant ($p < 0.001$). Officers exhibited the most disease, followed by enlisted flyers, then enlisted groundcrew. Participants with peach skin colors had a significantly higher history of non-melanoma than those with non-peach skin colors ($p=0.031$). Lighter hair color groups displayed significantly more nonmelanoma ($p=0.042$). Both reaction of skin to sun variables, after at least 2 hours and after repeated exposure, were significantly associated with nonmelanoma ($p < 0.001$ for each). History of nonmelanoma increased as burning or freckling potential among participants increased. The direct relationship with the composite sun reaction index was significant ($p < 0.001$) as well as the relationship with average lifetime residential latitude ($p < 0.001$). A history of nonmelanoma was higher for participants in the more southerly latitudes.

Each melanoma-by-covariate test of association was nonsignificant ($p > 0.10$ for each test).

A history of a systemic neoplasm and a history of a malignant systemic neoplasm each were tested separately for association with the appropriate covariates and the results were

similar. Both were associated with age ($p<0.001$ for both), where older participants displayed the higher percentages of systemic neoplasms and malignant systemic neoplasms. Both variables also were significantly associated with industrial chemical exposure ($p=0.003$ and $p=0.033$ respectively), although both histories were higher among participants that indicated no exposure. Lifetime cigarette smoking also was significantly associated with each variable ($p=0.031$ and $p=0.003$ respectively). Percentages of histories of both were highest among those participants who had smoked the greatest number of cigarettes. Additionally, a significant association between malignant systemic neoplasms and occupation was identified ($p<0.001$). Enlisted flyers displayed the highest history among the occupational categories.

The benign systemic neoplasms variable was significantly associated with age ($p<0.001$) and industrial chemical exposure ($p=0.012$). The association with age revealed a greater history of a benign skin neoplasm for the older participants, and the industrial chemical association indicated a greater history among those who were not exposed.

Only the association with occupation was significant of all the covariate association tests involving systemic neoplasms of uncertain behavior or unspecified nature ($p=0.043$). Officers exhibited the highest history among the occupational categories.

The ability to detect significant associations between covariates and site-specific history of malignant systemic neoplasms was lessened due to the sparse number of participants with a systemic neoplasm at a given site. Age was the only covariate considered significantly associated with a malignant systemic neoplasm of the eye, ear, face, head, or neck ($p=0.021$). Older participants exhibited a higher history of a malignant systemic neoplasm at these sites.

No tests of association were significant for the malignant systemic neoplasms of the oral cavity, pharynx, or larynx ($p>0.07$ for each test) and for malignant systemic neoplasms of the esophagus ($p>0.07$ for each test).

Lifetime alcohol history was significantly associated with malignant systemic neoplasms of the brain ($p=0.017$) although, history was highest within the 0 drink-years category.

Both malignant systemic neoplasms of the thymus, heart, or mediastinum and malignant systemic neoplasms of the thyroid gland did not demonstrate significant association with any covariate ($p>0.25$ and $p>0.21$ respectively for each test).

Tests of association involving malignant systemic neoplasms of the bronchus or lung revealed a significant and direct relationship with lifetime cigarette smoking history ($p=0.008$). Malignant systemic neoplasms of the bronchus or lung increased as the history of cigarette smoking increased.

No significant covariate associations with a history of malignant systemic neoplasms of the colon or rectum were found ($p>0.11$ for each test).

The malignant systemic neoplasms of the kidney or bladder variable was significantly associated with lifetime cigarette smoking history ($p=0.027$) and lifetime alcohol history ($p=0.014$). Neoplasms increased as both cigarette smoking and alcohol consumption increased. Insecticide exposure also was found to be significantly associated with malignant systemic neoplasms of the kidney or bladder ($p=0.049$), with more kidney or bladder neoplasms among participants who indicated no exposure.

Age and occupation were each significantly related to malignant systemic neoplasms of the prostate ($p<0.001$ and $p=0.001$ respectively). Disease was highest among older participants and officers.

All covariate association tests were nonsignificant for malignant systemic neoplasms of the testicles ($p>0.12$ for each test), ill-defined sites ($p>0.21$ for each test), and connective and other soft tissues ($p>0.25$ for each test). Tests involving carcinoma in situ of the penis and other unspecified sites and Hodgkin's disease also were nonsignificant ($p>0.48$ for each test and $p\geq 0.07$ for each test respectively).

Leukemia and lifetime alcohol history were significantly associated and inversely related ($p=0.032$), with less leukemia as alcohol consumption increased.

Non-Hodgkin's lymphoma, other malignant neoplasms of lymphoid and histiocytic tissue, and multiple myeloma did not exhibit any significant covariate association ($p>0.19$, $p>0.05$, and $p>0.32$ for each test respectively).

Age, occupation, skin color, eye color, lifetime alcohol history, industrial chemical exposure, and herbicide exposure each were significantly associated with skin or systemic neoplasms. Increases in skin or systemic neoplasms occurred as age ($p<0.001$), occupation ($p=0.001$; officers exhibited the highest history), and alcohol consumption ($p=0.046$) increased. A history of skin or systemic neoplasms was significantly associated with skin and eye color ($p=0.002$ and $p=0.005$ respectively). Participants with hazel or green eyes exhibited the highest history among all eye color categories. Participants with peach skin color displayed a higher history of neoplasms than participants with non-peach skin colors. The industrial chemical exposure association revealed a significantly higher percentage of participants with skin or systemic neoplasms who indicated no exposure ($p=0.031$), while those who indicated herbicide exposure exhibited the higher history of skin or systemic neoplasms ($p=0.015$). Because these were all associated with skin neoplasms and skin neoplasms accounted for the majority of total neoplasms, this observation is not unexpected.

Tests of covariate association were performed for both the continuous and discrete forms of PSA. The continuous measurement was associated with age ($p<0.001$), occupation ($p<0.001$), and ionizing radiation exposure ($p=0.007$). Prostate-specific antigen levels increased as age increased, and means were highest for officers. Significantly higher PSA means were revealed for participants who reported exposure to ionizing radiation.

The proportion of PSA measurements below the test sensitivity limit was not associated with any of the candidate covariates.

PSA discretized as normal or abnormal also was significantly associated with age ($p<0.001$). The higher percentage of abnormal levels were among older participants. In contrast to the continuous association test, race was significantly associated with PSA ($p=0.009$), with a higher percentage of abnormal levels in Blacks. Enlisted flyers also demonstrated the highest percentage of abnormal PSA levels within the three occupational cohorts ($p=0.003$). Ionizing radiation also was significantly related to the PSA ($p=0.016$). Participants who reported ionizing radiation exposure exhibited the higher prevalence of abnormalities.

In summary, age was significantly associated with many of the skin neoplasm and composite systemic neoplasm dependent variables. Race was significantly associated only with prostate-specific antigen. Occupation also was significantly associated with many of the skin neoplasm and composite systemic neoplasm dependent variables, probably due to the tendency of the officers to be older than the enlisted men in this study.

Skin neoplasms, malignant skin neoplasms, nonmelanomas, and skin or systemic neoplasms variables were significantly related to skin color. Hair color was significantly related only to basal cell carcinoma of the eye, ear, face, head, or neck and nonmelanoma. Eye color was only associated with skin or systemic neoplasms. The reaction of skin to sun variables, after at least 2 hours, after repeated exposure, and the composite index, were significantly associated with many of the skin neoplasm variables, primarily due to the associations with basal cell carcinoma. Similar patterns also were observed with average lifetime residential latitude.

Systemic neoplasms, malignant systemic neoplasms, and malignant systemic neoplasms of the bronchus or lung, and kidney or bladder variables each showed a significant association with lifetime cigarette smoking history. Lifetime alcohol history was associated with malignant systemic neoplasms of the brain and kidney or bladder, leukemia, and skin or systemic neoplasms.

The carcinogen covariates were related to only a few of the neoplasia dependent variables. Asbestos exposure was related only to basal cell carcinomas of the trunk and ionizing radiation exposure was associated with only the continuous and discrete prostate-specific antigen variables. Industrial chemical exposure was significantly associated with four variables: systemic neoplasms, malignant systemic neoplasms, benign systemic neoplasms, and skin or systemic neoplasms. Herbicide exposure was only significantly associated with skin or systemic neoplasms and insecticide exposure exhibited a significant association only with malignant systemic neoplasms of the kidney or bladder. Degreasing chemical exposure was not significantly associated with any of the neoplasia dependent variables.

Exposure Analysis

The following section presents the results of the statistical analyses of the dependent variables shown in Table 10-1. Dependent variables are grouped into two sections: those derived and verified from a review of medical records and the 1992 physical examination and data derived from the laboratory portion of the 1992 followup examination.

Unadjusted and adjusted analyses of six models are presented for each variable. Model 1 examines the relationship between the dependent variable and group (Ranch Hand or Comparison). Model 2 explores the relationship between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt. If a participant did not have a 1987 dioxin level, a 1992 level was used. A statistical adjustment for the percent of body fat at the participant's time of duty in SEA and the change in the percent of body fat from the time of duty in SEA to the date of the blood draw for dioxin is included in this model to account for body-fat-related differences in elimination rate (55). Model 3 dichotomizes the Ranch Hands in Model 2 based on their initial dioxin measures; these two categories of Ranch Hands are referred to as the "low Ranch Hand" category and the "high Ranch Hand" category. These participants are added to Ranch Hands and Comparisons with current serum dioxin levels (1987, if available; 1992, if the 1987 level was not available) at or below 10 ppt to create a total of four categories. Ranch Hands with current serum dioxin levels at or below 10 ppt are referred to as the "background Ranch Hand" category. The relationship between the dependent variable in each of the three Ranch Hand categories and the dependent variable in the "Comparison" category is examined. A fourth contrast, exploring the relationship of the dependent variable in the low Ranch Hand category and the high Ranch Hand category combined, also is conducted. This combination is referred to in the text and tables as the "low plus high Ranch Hand" category. As in Model 2, a statistical adjustment is made for the percent of body fat at the participant's time of duty in SEA and the change in the percent of body fat from the time of duty in SEA to the date of the blood draw for dioxin.

Models 4, 5, and 6 examine the relationship between the dependent variable and 1987 dioxin levels in all Ranch Hands with a dioxin measurement. If a participant did not have a 1987 dioxin measurement, a 1992 measurement was utilized in determining the current dioxin level. The measure of dioxin in Model 4 is lipid-adjusted, whereas whole-weight dioxin is used in Models 5 and 6. Model 6 differs from Model 5 in that a statistical adjustment for total lipids is included in Model 6. Details on dioxin and the modeling strategy are found in Chapters 2 and 7 respectively.

Results of investigation for group-by-covariate and dioxin-by-covariate interactions are referenced in the text, and tabular results are presented in Appendix F-2.

Verified Medical Records Variables

Skin Neoplasms

The Model 1 unadjusted and adjusted analyses revealed marginally significant associations between group and a history of a skin neoplasm (Table 10-3(a,b): $p=0.095$, Est. $RR=1.18$ and $p=0.074$, Adj. $RR=1.19$ respectively). Histories of a skin neoplasm were 31.6 percent for Ranch Hands and 28.1 percent for Comparisons. All unadjusted and adjusted contrasts within each occupational category were nonsignificant (Table 10-3(a,b): $p>0.22$ for all remaining contrasts). Significant covariates include age, skin color, reaction of skin to sun after at least 2 hours, average lifetime residential latitude, and ionizing radiation exposure.

Table 10-3.
Analysis of Skin Neoplasms

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***886***	***31.6***	***1.18 (0.98,1.43)***	***0.095***
	Comparison	***1,198***	***28.1***		
Officer	Ranch Hand	357	35.6	1.18 (0.89,1.58)	0.287
	Comparison	490	31.8		
Enlisted Flyer	Ranch Hand	150	31.3	1.29 (0.80,2.07)	0.360
	Comparison	187	26.2		
Enlisted Groundcrew	Ranch Hand	379	28.0	1.14 (0.85,1.54)	0.419
	Comparison	521	25.3		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.19 (0.98,1.45)***	***0.074***	AGE ($p<0.001$)
Officer	1.20 (0.90,1.61)	0.221	SKIN ($p=0.072$)
Enlisted Flyer	1.32 (0.81,2.15)	0.259	SUN2HR ($p<0.001$)
Enlisted Groundcrew	1.14 (0.85,1.55)	0.382	LAT ($p=0.104$)
			IONRAD ($p=0.145$)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 10-3. (Continued)
Analysis of Skin Neoplasms

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	152	35.5	0.77 (0.66,0.90)	<0.001
Medium	161	29.8		
High	164	24.4		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
	Analysis Results for Log_2 (Initial Dioxin)[c]		
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
476	0.76 (0.64,0.89)	<0.001	EYE (p=0.082) SUN2HR (p<0.001) IC (p=0.088)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-3. (Continued)
Analysis of Skin Neoplasms

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,002	28.3		
Background RH	356	33.4	1.31 (1.01,1.70)	0.043
Low RH	232	36.6	1.44 (1.06,1.94)	0.019
High RH	245	23.3	0.75 (0.54,1.04)	0.083
Low plus High RH	477	29.8	1.05 (0.82,1.34)	0.694

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	988			AGE (p=0.031) SKIN (p=0.047) SUN2HR (p=0.007) LAT (p=0.115)
Background RH	354	1.26 (0.96,1.64)	0.090	
Low RH	229	1.44 (1.06,1.96)	0.021	
High RH	245	0.79 (0.57,1.11)	0.170	
Low plus High RH	474	1.08 (0.85,1.38)	0.526	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 10-3. (Continued)
Analysis of Skin Neoplasms

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	33.1 (281)	36.8 (272)	24.3 (280)	0.88 (0.79,0.97)	0.011
5	33.0 (285)	33.6 (268)	27.5 (280)	0.92 (0.85,1.01)	0.065
6[c]	33.1 (284)	33.6 (268)	27.5 (280)	0.86 (0.78,0.95)	0.002

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	832	0.90 (0.81,1.00)	0.056	AGE (p=0.069) SUN2HR (p=0.009)
5	831	0.94 (0.86,1.03)**	0.175**	CURR*SKIN (p=0.020) CURR*IC (p=0.033) AGE (p=0.043) SUN2HR (p=0.008)
6[d]	830	0.88 (0.79,0.97)**	0.008**	CURR*SKIN (p=0.022) CURR*IC (p=0.040) AGE (p=0.089) SUN2HR (p=0.005)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interactions ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table F-2-1 for further analysis of these interactions.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.
CURR: Log_2 (current dioxin + 1).

Highly significant results were revealed from the Model 2 unadjusted and adjusted analyses of a history of a skin neoplasm (Table 10-3(c,d): $p<0.001$, Est. RR=0.77 and $p<0.001$, Adj. RR=0.76 respectively). The relative risks, which were less than one, indicate that the history of a skin neoplasm decreased as initial dioxin levels increased. Eye color, reaction of skin to sun after at least 2 hours, and industrial chemical exposure were significant in the Model 2 final adjusted model.

Unadjusted contrasts between Comparisons and background Ranch Hands and between Comparisons and low Ranch Hands in Model 3 revealed significant differences (Table 10-3(e): $p=0.043$, Est. RR=1.31 and $p=0.019$, Est. RR=1.44 respectively). For Comparisons, 28.3 percent had a history of a skin neoplasm. For Ranch Hands in the background category, 33.4 percent had a history of a skin neoplasm, and 36.6 percent of Ranch Hands in the low category had a history of a skin neoplasm. The percentage of Ranch Hands in the high category with a history of a skin neoplasm (23.3%) was marginally significantly less than Comparisons (Table 10-3(e): $p=0.083$, Est. RR=0.75). After adjustment for covariates, the difference between Comparisons and background Ranch Hands was marginally significant (Table 10-3(f): $p=0.090$, Adj. RR=1.26). The contrast between Comparisons and low Ranch Hands remained significant after covariate adjustment (Table 10-3(f): $p=0.021$, Adj. RR=1.44), and the contrast between Comparisons and Ranch Hands in the high category became nonsignificant ($p=0.170$). Model 3 adjusted for age, skin color, reaction of skin to sun after at least 2 hours, and average lifetime residential latitude. The unadjusted and adjusted low plus high Ranch Hand contrasts were nonsignificant (Table 10-3(e,f); $p>0.52$ for each contrast).

Significant associations were found between current dioxin and the history of a skin neoplasm from the unadjusted analyses of Models 4 and 6 (Table 10-3(g): $p=0.011$, Est. RR=0.88 and $p=0.002$, Est. RR=0.86). The percentage of Ranch Hands with a history of a skin neoplasm decreased as current dioxin increased. The Model 5 unadjusted result was marginally significant and exhibited a similar relationship between a history of a skin neoplasm and current dioxin (Table 10-3(g): $p=0.065$, Est. RR=0.92). Analysis of Model 4 was marginally significant after adjusting for the effects of age and reaction of skin to sun after at least 2 hours (Table 10-3(h): $p=0.056$, Adj. RR=0.90). Models 5 and 6 each adjusted for age, reaction of skin to sun after at least 2 hours, and the interactions of current dioxin-by-skin color and current dioxin-by-industrial chemical exposure. Stratified results for each level of each interaction are presented in Appendix Table F-2-1. After deletion of the interactions from the final adjusted models, the association between a history of a skin neoplasm and current dioxin was nonsignificant in Model 5 (Table 10-3(h): $p=0.175$). For Model 6, the results after adjustment for the covariates revealed a highly significant association. Similarly, the percentage of Ranch Hands with a history of a skin neoplasm decreased as current dioxin increased (Table 10-3(h): $p=0.008$, Adj. RR=0.88).

Malignant Skin Neoplasms

All Model 1 differences between Ranch Hands and Comparisons from the unadjusted and adjusted analyses of a history of a malignant skin neoplasm were statistically nonsignificant (Table 10-4(a,b): $p>0.22$ for all contrasts). Covariates in the final adjusted model were age, reaction of skin to sun after at least 2 hours, reaction of skin to sun after repeated exposure, and average lifetime residential latitude.

Table 10-4.
Analysis of Malignant Skin Neoplasms

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***886***	***13.5***	***1.16 (0.89,1.50)***	***0.305***
	Comparison	***1,198***	***11.9***		
Officer	Ranch Hand	357	18.5	1.26 (0.87,1.80)	0.257
	Comparison	490	15.3		
Enlisted Flyer	Ranch Hand	150	14.7	1.23 (0.65,2.30)	0.636
	Comparison	187	12.3		
Enlisted Groundcrew	Ranch Hand	379	8.4	0.98 (0.61,1.57)	0.999
	Comparison	521	8.6		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.17 (0.90,1.54)***	***0.244***	AGE ($p<0.001$)
Officer	1.26 (0.87,1.84)	0.228	SUN2HR ($p<0.001$)
Enlisted Flyer	1.29 (0.67,2.46)	0.445	SUNRPT ($p<0.001$)
Enlisted Groundcrew	0.99 (0.61,1.61)	0.972	LAT ($p=0.003$)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 10-4. (Continued)
Analysis of Malignant Skin Neoplasms

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	152	16.5	0.74 (0.59,0.93)	0.006
Medium	161	13.0		
High	164	8.5		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
472	****	****	INIT*INS (p=0.007) AGE (p=0.108) SUN2HR (p=0.099) SUNRPT (p=0.007) LAT (p=0.054)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

**** Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.01$); adjusted relative risk, confidence interval, and p-value not presented; refer to Appendix Table F-2-2 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
INIT = Log_2 (initial dioxin).

Table 10-4. (Continued)
Analysis of Malignant Skin Neoplasms

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,002	11.7		
Background RH	356	14.3	1.33 (0.93,1.90)	0.119
Low RH	232	17.3	1.53 (1.03,2.26)	0.036
High RH	245	8.2	0.65 (0.39,1.07)	0.089
Low plus High RH	477	12.6	1.05 (0.75,1.47)	0.761

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	984			DXCAT*IC (p=0.048) DXCAT*INS (p=0.036) AGE (p<0.001) SUN2HR (p=0.004) SUNRPT (p=0.002) LAT (p=0.003)
Background RH	354	1.19 (0.82,1.73)**	0.355**	
Low RH	228	1.45 (0.96,2.20)**	0.077**	
High RH	244	0.79 (0.47,1.32)**	0.362**	
Low plus High RH	472	1.13 (0.79,1.60)**	0.509**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interactions ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table F-2-2 for further analysis of these interactions.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.
DXCAT = Categorized Dioxin.

Table 10-4. (Continued)
Analysis of Malignant Skin Neoplasms

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Yes/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	14.6 (281)	16.2 (272)	9.3 (280)	0.86 (0.75,1.00)	0.038
5	14.4 (285)	15.3 (268)	10.4 (280)	0.91 (0.81,1.03)	0.132
6[c]	14.4 (284)	15.3 (268)	10.4 (280)	0.86 (0.76,0.98)	0.021

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	829	0.94 (0.81,1.09)	0.428	AGE (p<0.001) SUN2HR (p=0.040) SUNRPT (p=0.010)
5	829	0.99 (0.87,1.12)	0.819	AGE (p<0.001) SUN2HR (p=0.039) SUNRPT (p=0.009)
6[d]	825	0.92 (0.80,1.06)	0.234	AGE (p<0.001) SUN2HR (p=0.032) SUNRPT (p=0.016) LAT (p=0.137)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Unadjusted analysis of Model 2 indicated a decrease in a history of a malignant skin neoplasm with increasing levels of initial dioxin (Table 10-4(c): p=0.006, Est. RR=0.74). Model 3 unadjusted analysis revealed a significant difference between Comparisons and low Ranch Hands (Table 10-4(e): p=0.036, Est. RR=1.53). For Comparisons, 11.7 percent had a history of a malignant skin neoplasm, whereas 17.3 percent of low Ranch Hands had a history of a malignant skin neoplasm. There also was a marginally significant difference between the percentage of Ranch Hands in the high dioxin category with a history of a malignant skin neoplasm (8.2%) and Comparisons (Appendix Table 10-4(e): p=0.089, Est. RR=0.65). Other contrasts were nonsignificant (Table 10-4(e): p>0.11 for all remaining contrasts).

Models 2 and 3 both adjusted for a dioxin-by-insecticide exposure interaction, age, reaction of skin to sun after at least 2 hours, reaction of skin to sun after repeated exposure, and average lifetime residential latitude. Model 3 also adjusted for the interaction of categorized dioxin-by-industrial chemical exposure. Stratified results are presented in Appendix F-2-2 for each level of each interaction.

From Model 2 results stratified by insecticide exposure (no, yes), a highly significant association between initial dioxin and a history of a malignant skin neoplasm was revealed for Ranch Hands who reported insecticide exposure (Appendix Table F-2-2(a): p=0.004, Adj. RR=0.64). The percentage of Ranch Hands with a history of a malignant skin neoplasm decreased as initial dioxin increased. After deletion of the interactions from the final model of Model 3, the low Ranch Hand category versus Comparison category contrast was marginally significant (Table 10-4(f): p=0.077, Adj. RR=1.45). All other Model 3 adjusted contrasts were nonsignificant (Table 10-4(f): p>0.35 for all remaining contrasts).

Unadjusted analyses for Models 4 and 6 were significant and also indicated that the percentage of Ranch Hands with a history of a malignant skin neoplasm decreased as current dioxin increased (Table 10-4(g): p=0.038, Est. RR=0.86 and p=0.021, Est. RR=0.86 respectively). The Model 5 unadjusted analysis and the adjusted analyses for Models 4, 5, and 6 were nonsignificant (Table 10-4(g,h): p>0.13 for all analyses). Each final model adjusted for age, reaction of skin to sun after at least 2 hours, and reaction of skin to sun after repeated exposure. Model 6 also adjusted for average lifetime residential latitude.

Benign Skin Neoplasms

The Model 1 analysis of benign skin neoplasms showed nonsignificant differences between Ranch Hands and Comparisons for all unadjusted and adjusted contrasts (Table 10-5(a,b): p>0.10 for all contrasts). No significant covariates were detected in the adjusted analysis.

The Model 2 analyses revealed a marginally significant decrease in the history of a benign skin neoplasm as initial dioxin increased (Table 10-5(c): p=0.085, Est. and Adj. RR=0.86). Conversely, the contrast of Comparisons and background Ranch Hands of Model 3 revealed more background Ranch Hands (21.6%) had a history of a benign skin neoplasm than Comparisons (17.6%), resulting in a marginally significant increase (Table 10-5(e,f): p=0.082, Est. and Adj. RR=1.30). All remaining Model 3 contrasts were

Table 10-5.
Analysis of Benign Skin Neoplasms

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***942***	***20.1***	***1.20 (0.97,1.49)***	***0.109***
	Comparison	***1,272***	***17.3***		
Officer	Ranch Hand	364	20.6	1.19 (0.84,1.67)	0.372
	Comparison	496	17.9		
Enlisted Flyer	Ranch Hand	160	19.4	1.56 (0.89,2.74)	0.160
	Comparison	202	13.4		
Enlisted Groundcrew	Ranch Hand	418	19.9	1.12 (0.81,1.54)	0.543
	Comparison	574	18.1		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
All	***1.20 (0.97,1.49)***	***0.109***	
Officer	1.19 (0.84,1.67)	0.372	
Enlisted Flyer	1.56 (0.89,2.74)	0.160	
Enlisted Groundcrew	1.12 (0.81,1.54)	0.543	

Table 10-5. (Continued)
Analysis of Benign Skin Neoplasms

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	169	20.7	0.86 (0.72,1.02)	0.085
Medium	171	17.0		
High	173	17.3		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[a]			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
513	0.86 (0.72,1.02)	0.085	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-5. (Continued)
Analysis of Benign Skin Neoplasms

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,056	17.6		
Background RH	371	21.6	1.30 (0.97,1.75)	0.082
Low RH	255	20.0	1.17 (0.83,1.66)	0.365
High RH	258	16.7	0.92 (0.64,1.33)	0.661
Low plus High RH	513	18.3	1.04 (0.79,1.38)	0.761

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ab]	p-Value	Covariate Remarks
Comparison	1,056			
Background RH	371	1.30 (0.97,1.75)	0.082	
Low RH	255	1.17 (0.83,1.66)	0.365	
High RH	258	0.92 (0.64,1.33)	0.661	
Low plus High RH	513	1.04 (0.79,1.38)	0.761	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 10-5. (Continued)
Analysis of Benign Skin Neoplasms

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Yes/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	20.8 (293)	22.1 (294)	16.2 (297)	0.90 (0.80,1.01)	0.082
5	20.8 (298)	20.6 (291)	17.6 (295)	0.93 (0.85,1.03)	0.160
6[c]	20.9 (297)	20.6 (291)	17.6 (295)	0.89 (0.80,0.99)	0.029

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	n	Analysis Results for Log_2 (Current Dioxin + 1) Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	884	0.88 (0.78,0.99)	0.034	DC (p=0.067)
5	883	0.91 (0.82,1.01)**	0.075**	CURR*SKIN (p=0.013) DC (p=0.087)
6[d]	882	0.87 (0.78,0.97)**	0.012**	CURR*SKIN (p=0.015) DC (p=0.078)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table F-2-3 for further analysis of this interaction.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

nonsignificant (Table 10-5(e,f): $p > 0.36$ for all remaining contrasts). Similar to Model 1, Models 2 and 3 retained no significant covariates in the final model.

A marginally significant association was found from the Model 4 analysis, where the history of a benign skin neoplasm decreased as current dioxin increased (Table 10-5(g): $p=0.082$, Est. RR=0.90). After adjustment for degreasing chemical exposure, the association became significant (Table 10-5(h): $p=0.034$, Adj. RR=0.88). Unadjusted analysis of Model 5 was nonsignificant (Table 10-5(g): $p=0.160$). The Model 6 unadjusted analysis was significant; again, the history of a benign skin neoplasm decreased as current dioxin increased (Table 10-5(g): $p=0.029$, Est. RR=0.89). Analyses of Models 5 and 6 adjusted for degreasing chemical exposure and a current dioxin-by-skin color interaction. Appendix Table F-2-3 contains results stratified by skin color. After deletion of each interaction from each final model, the association between current dioxin and benign skin neoplasms was marginally significant in Model 5 and significant in Model 6 (Table 10-5(g,h): $p=0.075$, Adj. RR=0.91 and $p=0.012$, Adj. RR=0.87 respectively).

Skin Neoplasms of Uncertain Behavior or Unspecified Nature

All Model 1 unadjusted and adjusted contrasts were nonsignificant (Table 10-6(a,b): $p > 0.85$ for all contrasts). Analyses were not performed for the enlisted flyers, because no participant had a history of a skin neoplasm of uncertain behavior or unspecified nature. Reaction of skin to sun after repeated exposure was significant in the final adjusted model.

All results from the unadjusted analyses of Models 2 and 3 and the adjusted analyses of Model 3 of skin neoplasms of uncertain behavior or unspecified nature were nonsignificant (Table 10-6(c-f): $p > 0.53$ for all analyses). Adjusted analyses for Model 2 were not possible because of the sparseness of participants with a history of a skin neoplasm of uncertain behavior or unspecified nature (n=2). Significant covariates retained in Model 3 were eye color and reaction of skin to sun after repeated exposure.

No significant relationship was found between current dioxin and skin neoplasms of uncertain behavior or unspecified nature for the unadjusted analyses of Models 4, 5, and 6 (Table 10-6(g,h): $p > 0.78$ for each analysis). Similar to Model 2, adjusted analyses were not performed because of the sparse number of Ranch Hands with a history of a skin neoplasm of uncertain behavior or unspecified nature (n=4 for Models 4, 5, and 6).

Basal Cell Carcinomas (All Sites Combined)

No significant differences were found between Ranch Hands and Comparisons for the unadjusted and adjusted analyses of basal cell carcinomas (all sites combined) (Table 10-7(a,b): $p > 0.39$ for all contrasts). Significant covariates from the adjusted analyses were age, reaction of skin to sun after at least 2 hours, reaction of skin to sun after repeated exposure, average lifetime residential latitude, and insecticide exposure.

Unadjusted and adjusted analyses of Model 2 indicated a significant association between initial dioxin and basal cell carcinomas (all sites combined), where the history of a basal cell carcinoma decreased as initial dioxin increased (Table 10-7(c,d): $p=0.013$, Est. RR=0.75

Table 10-6.
Analysis of Skin Neoplasms of Uncertain Behavior or Unspecified Nature

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***886***	***0.5***	***0.77 (0.23,2.64)***	***0.914***
	Comparison	***1,198***	***0.6***		
Officer	Ranch Hand	357	0.6	0.92 (0.15,5.50)	0.999
	Comparison	490	0.6		
Enlisted Flyer	Ranch Hand	150	0.0	--	--
	Comparison	187	0.0		
Enlisted Groundcrew	Ranch Hand	379	0.5	0.69 (0.13,3.76)	0.982
	Comparison	521	0.8		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***0.89 (0.25,3.17)***	***0.854***	SUNRPT (p=0.011)
Officer	0.88 (0.14,5.32)	0.886	
Enlisted Flyer	--	--	
Enlisted Groundcrew	0.96 (0.16,5.77)	0.960	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

--: Adjusted relative risk, confidence interval, and p-value not presented due to zero abnormalities.

Table 10-6. (Continued)
Analysis of Skin Neoplasms of Uncertain Behavior or Unspecified Nature

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	152	0.7	0.72 (0.24,2.15)	0.530
Medium	161	0.6		
High	164	0.0		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
--	--	--	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

--: Adjusted analysis not performed due to the sparse number of abnormalities.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-6. (Continued)
Analysis of Skin Neoplasms of Uncertain Behavior or Unspecified Nature

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,002	0.5		
Background RH	356	0.6	1.30 (0.25,6.85)	0.760
Low RH	232	0.4	0.79 (0.09,6.90)	0.830
High RH	245	0.4	0.69 (0.08,6.09)	0.739
Low plus High RH	477	0.4	0.74 (0.14,3.90)	0.719

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	994			EYE (p=0.129) SUNRPT (p=0.032)
Background RH	355	1.42 (0.26,7.65)	0.685	
Low RH	230	0.76 (0.09,6.74)	0.805	
High RH	244	0.69 (0.08,6.07)	0.738	
Low plus High RH	474	0.72 (0.14,3.81)	0.702	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 10-6. (Continued)
Analysis of Skin Neoplasms of Uncertain Behavior or Unspecified Nature

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.4 (281)	0.7 (272)	0.4 (280)	0.91 (0.46,1.82)	0.789
5	0.7 (285)	0.4 (268)	0.4 (280)	0.93 (0.52,1.64)	0.790
6[c]	0.7 (284)	0.4 (268)	0.4 (280)	0.96 (0.52,1.79)	0.896

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
4	--	--	--	
5	--	--	--	
6	--	--	--	

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

--: Adjusted analysis not performed due to the sparse number of abnormalities.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 10-7.
Analysis of Basal Cell Carcinomas (All Sites Combined)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***886***	***11.3***	***1.12 (0.85,1.49)***	***0.462***
	Comparison	***1,198***	***10.2***		
Officer	Ranch Hand	357	15.1	1.21 (0.82,1.79)	0.399
	Comparison	490	12.9		
Enlisted Flyer	Ranch Hand	150	13.3	1.22 (0.63,2.34)	0.675
	Comparison	187	11.2		
Enlisted Groundcrew	Ranch Hand	379	6.9	0.94 (0.56,1.57)	0.906
	Comparison	521	7.3		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.11 (0.82,1.48)***	***0.502***	AGE ($p<0.001$)
Officer	1.18 (0.78,1.77)	0.434	SUN2HR ($p<0.001$)
Enlisted Flyer	1.24 (0.63,2.44)	0.541	SUNRPT ($p=0.002$)
Enlisted Groundcrew	0.93 (0.54,1.58)	0.778	LAT ($p<0.001$)
			INS ($p=0.107$)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 10-7. (Continued)
Analysis of Basal Cell Carcinomas (All Sites Combined)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	152	13.8	0.75 (0.59,0.95)	0.013
Medium	161	11.8		
High	164	6.1		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
474	0.75 (0.57,0.97)	0.023	AGE (p=0.068) HAIR (p=0.101) SUN2HR (p=0.003) LAT (p=0.031)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-7. (Continued)
Analysis of Basal Cell Carcinomas (All Sites Combined)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,002	10.1		
Background RH	356	11.8	1.25 (0.85,1.84)	0.254
Low RH	232	14.7	1.48 (0.97,2.25)	0.066
High RH	245	6.5	0.60 (0.35,1.04)	0.071
Low plus High RH	477	10.5	1.01 (0.71,1.45)	0.948

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	984			AGE ($p<0.001$) SUN2HR ($p<0.001$) SUNRPT ($p=0.004$) LAT ($p<0.001$) INS ($p=0.041$)
Background RH	354	1.12 (0.75,1.67)	0.593	
Low RH	228	1.41 (0.91,2.20)	0.126	
High RH	244	0.71 (0.40,1.25)	0.238	
Low plus High RH	472	1.07 (0.73,1.56)	0.732	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 10-7. (Continued)
Analysis of Basal Cell Carcinomas (All Sites Combined)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Yes/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	12.5 (281)	12.9 (272)	7.9 (280)	0.86 (0.74,1.01)	0.057
5	11.9 (285)	12.7 (268)	8.6 (280)	0.91 (0.81,1.04)	0.166
6[c]	12.0 (284)	12.7 (268)	8.6 (280)	0.86 (0.75,0.99)	0.032

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	n	Analysis Results for Log_2 (Current Dioxin + 1) Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	826	0.93 (0.79,1.09)	0.350	AGE (p=0.002) SUN2HR (p=0.056) SUNRPT (p=0.040) LAT (p=0.028)
5	826	0.97 (0.85,1.11)	0.669	AGE (p=0.001) SUN2HR (p=0.055) SUNRPT (p=0.037) LAT (p=0.030)
6[d]	825	0.91 (0.78,1.05)**	0.194**	CURR*ASB (p=0.027) AGE (p=0.001) SUN2HR (p=0.030) SUNRPT (p=0.024) LAT (p=0.021)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table F-2-4 for further analysis of this interaction.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

and p=0.023, Adj. RR=0.75 respectively). Age, hair color, reaction of skin to sun after at least 2 hours, and average lifetime residential latitude were significant covariates. Model 3 unadjusted analyses revealed a marginally significant difference between Ranch Hands in the low dioxin category and Comparisons (Table 10-7(e): p=0.066, Est. RR=1.48). More Ranch Hands in the low dioxin category (11.8%) had a history of a basal cell carcinoma than Comparisons (10.1%). The contrast between Ranch Hands in the high dioxin category and Comparisons also was marginally significant (p=0.071, Est. RR=0.60). Of Ranch Hands in the high dioxin category, 6.5 percent exhibited a history of a basal cell carcinoma. All remaining unadjusted contrasts and all adjusted contrasts for Model 3 were nonsignificant (Table 10-7(e,f): p>0.12 for each contrast). Significant covariates included age, reaction of skin to sun after at least 2 hours, reaction of skin to sun after repeated exposure, average lifetime residential latitude, and insecticide exposure.

Unadjusted analyses relating the history of basal cell carcinoma to current dioxin revealed a marginally significant association for Model 4 and a significant association for Model 6. In both analyses, the history of a basal cell carcinoma decreased as current dioxin increased (Table 10-7(g): p=0.057, Est. RR=0.86 and p=0.032, Est. RR=0.86 respectively). The unadjusted analysis for Model 5 was nonsignificant (Table 10-7(g): p=0.166). All results from the adjusted analyses of Models 4, 5, and 6 also were nonsignificant (Table 10-7(h): p>0.19 for all adjusted analyses). Each model adjusted for age, reaction of skin to sun after at least 2 hours, reaction of skin to sun after repeated exposure, and average lifetime residential latitude. The current dioxin-by-asbestos exposure interaction also was significant in Model 6. The results displayed in Table 10-7(h) are from the final model after this interaction was deleted. Results stratified by each level of asbestos exposure are displayed in Appendix Table F-2-4.

Basal Cell Carcinomas (Ear, Face, Head, and Neck)

All unadjusted and adjusted Model 1 analyses of basal cell carcinomas on the ear, face, head, or neck were nonsignificant (Table 10-8(a,b): p>0.19 for all contrasts). Age, reaction of skin to sun after at least 2 hours after first exposure, reaction of skin to sun after repeated exposure, and average lifetime residential latitude were retained in the final adjusted model.

The Model 2 unadjusted and adjusted analysis of basal cell carcinomas on the ear, face, head, or neck revealed significant associations with initial dioxin (Table 10-8(c,d): p=0.017, Est. RR=0.73 and p=0.006, Adj. RR=0.68). The history of a basal cell carcinoma on these sites decreased as levels of current dioxin increased. Significant covariates were reaction of skin to sun after at least 2 hours and average lifetime residential latitude.

A significant difference was found in the Model 3 unadjusted contrast between Ranch Hands in the low category and Comparisons (Table 10-8(e): p=0.042, Est. RR=1.61). For Ranch Hands in the low category, 12.1 percent exhibited a history of a basal cell carcinoma on the ear, face, head, or neck, as contrasted to 7.6 percent of Comparisons. Marginally significant differences were revealed between Comparisons and each of the background and high Ranch Hands categories (Table 10-8(e): p=0.091, Est. RR=1.44 and p=0.076, Est. RR=0.56 respectively). Adjusted contrasts exhibited a marginally significant difference between low Ranch Hands and Comparisons (Table 10-8(f): p=0.098, Adj. RR=1.51). All

Table 10-8.
Analysis of Basal Cell Carcinomas (Ear, Face, Head, and Neck)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***886***	***9.1***	***1.18 (0.87,1.61)***	***0.330***
	Comparison	***1,198***	***7.9***		
Officer	Ranch Hand	357	12.0	1.32 (0.85,2.05)	0.258
	Comparison	490	9.4		
Enlisted Flyer	Ranch Hand	150	10.7	1.12 (0.55,2.28)	0.894
	Comparison	187	9.6		
Enlisted Groundcrew	Ranch Hand	379	5.8	1.01 (0.57,1.78)	0.999
	Comparison	521	5.8		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.21 (0.88,1.68)***	***0.244***	AGE ($p<0.001$)
Officer	1.35 (0.86,2.14)	0.196	SUN2HR ($p<0.001$)
Enlisted Flyer	1.15 (0.55,2.42)	0.703	SUNRPT ($p=0.003$)
Enlisted Groundcrew	1.04 (0.58,1.86)	0.893	LAT ($p<0.001$)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 10-8. (Continued)
Analysis of Basal Cell Carcinomas (Ear, Face, Head, and Neck)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	152	10.5	0.73 (0.55,0.96)	0.017
Medium	161	10.6		
High	164	3.7		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
474	0.68 (0.51,0.92)	0.006	SUN2HR ($p<0.001$) LAT ($p=0.014$)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-8. (Continued)
Analysis of Basal Cell Carcinomas (Ear, Face, Head, and Neck)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,002	7.6		
Background RH	356	10.1	1.44 (0.94,2.19)	0.091
Low RH	232	12.1	1.61 (1.02,2.56)	0.042
High RH	245	4.5	0.56 (0.29,1.06)	0.076
Low plus High RH	477	8.2	1.05 (0.70,1.58)	0.812

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	984			AGE ($p<0.001$) SUN2HR ($p<0.001$) SUNRPT ($p=0.008$) LAT ($p<0.001$) INS ($p=0.063$)
Background RH	354	1.29 (0.84,2.00)	0.246	
Low RH	228	1.51 (0.93,2.46)	0.098	
High RH	244	0.68 (0.35,1.32)	0.256	
Low plus High RH	472	1.11 (0.73,1.70)	0.618	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 10-8. (Continued)
Analysis of Basal Cell Carcinomas (Ear, Face, Head, and Neck)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Yes/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	10.7 (281)	10.3 (272)	6.1 (280)	0.81 (0.68,0.97)	0.016
5	9.8 (285)	10.8 (268)	6.4 (280)	0.87 (0.76,1.00)	0.056
6[c]	9.9 (284)	10.8 (268)	6.4 (280)	0.82 (0.70,0.95)	0.009

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	826	0.88 (0.73,1.05)	0.151	AGE (p=0.002) SUN2HR (p=0.049) SUNRPT (p=0.087) LAT (p=0.040)
5	826	0.93 (0.81,1.08)	0.347	AGE (p=0.001) SUN2HR (p=0.049) SUNRPT (p=0.083) LAT (p=0.042)
6[d]	825	0.87 (0.74,1.02)	0.079	AGE (p=0.001) SUN2HR (p=0.031) SUNRPT (p=0.088) LAT (p=0.036)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

other contrasts were nonsignificant (Table 10-8(e,f): $p>0.24$ for all other contrasts). Age, reaction of skin to sun after at least 2 hours, reaction of skin to sun after repeated exposure, average lifetime residential latitude, and insecticide exposure were significant in the Model 3 adjusted analysis.

Analysis of associations between basal cell carcinomas on the ear, face, head, or neck and current dioxin were examined in Models 4, 5, and 6. Unadjusted results were significant for Models 4 and 6 and marginally significant for Model 5 (Table 10-8(g): Model 4: $p=0.016$, Est. RR=0.81; Model 6: $p=0.009$, Est. RR=0.82; and Model 5: $p=0.056$, Est. RR=0.87). Each analysis indicated a decrease in basal cell carcinomas on the ear, face, head, or neck from the Ranch Hands with increasing current dioxin levels. Results of the Model 6 adjusted analysis were marginally significant (Table 10-8(h): $p=0.079$, Adj. RR=0.87). Adjusted analyses of Models 4 and 5 were nonsignificant (Table 10-8(h): $p>0.15$ for each analysis). Each model retained age, reaction of skin to sun after at least 2 hours, reaction of skin to sun after repeated exposure, and average lifetime residential latitude in the final adjusted model.

Basal Cell Carcinomas (Trunk)

All unadjusted and adjusted contrasts examined from the Model 1 analysis of basal cell carcinomas on the trunk were nonsignificant (Table 10-9(a,b): $p>0.35$ for all contrasts). Adjusted analysis retained age, reaction of skin to sun after at least 2 hours after first exposure, reaction of skin to sun after repeated exposure, average lifetime residential latitude, asbestos exposure, and herbicide exposure in the final model.

Similar to Model 1, all Model 2 and 3 results obtained from the unadjusted and adjusted analysis of basal cell carcinomas on the trunk were nonsignificant (Table 10-9(c-f): $p>0.13$ for all analyses). Both models adjusted for the significant covariate effects of age, average lifetime residential latitude, and asbestos exposure. Model 3 also retained eye color, reaction of skin to sun after at least 2 hours, reaction of skin to sun after repeated exposure, herbicide exposure, and the interaction of categorized dioxin-by-insecticide exposure. Adjusted results are presented for Model 3 after deletion of this interaction from the final model. Results stratified by each level of insecticide exposure are presented in Appendix Table F-2-5.

Unadjusted and adjusted current dioxin analyses of basal cell carcinomas on the trunk were nonsignificant for Models 4, 5, and 6 (Table 10-9(g,h): $p>0.55$ for all analyses). Each model adjusted for the covariate effects of age, asbestos exposure, and the interaction of current dioxin-by-insecticide exposure. Model 4 also retained reaction of skin to sun after repeated exposure. All adjusted results displayed in Table 10-9 are from the final model after deletion of the current dioxin-by-insecticide exposure interaction. Results are presented by each level of insecticide exposure for each model in Appendix Table F-2-5.

Basal Cell Carcinomas (Upper Extremities)

All unadjusted and adjusted results from Model 1 analysis of basal cell carcinomas on the upper extremities were nonsignificant (Table 10-10(a,b): $p>0.48$ for all contrasts).

Table 10-9.
Analysis of Basal Cell Carcinomas (Trunk)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***886***	***3.5***	***1.17 (0.72,1.91)***	***0.613***
	Comparison	***1,198***	***3.0***		
Officer	Ranch Hand	357	5.6	1.21 (0.65,2.23)	0.663
	Comparison	490	4.7		
Enlisted Flyer	Ranch Hand	150	4.0	1.91 (0.53,6.88)	0.498
	Comparison	187	2.1		
Enlisted Groundcrew	Ranch Hand	379	1.3	0.76 (0.25,2.29)	0.829
	Comparison	521	1.7		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***0.90 (0.50,1.61)***	***0.714***	AGE ($p<0.001$)
Officer	0.92 (0.46,1.87)	0.823	SUN2HR ($p=0.014$) SUNRPT ($p=0.048$)
Enlisted Flyer	1.62 (0.43,6.17)	0.478	LAT ($p=0.030$) ASB ($p=0.021$)
Enlisted Groundcrew	0.58 (0.18,1.86)	0.359	HERB ($p=0.081$)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 10-9. (Continued)
Analysis of Basal Cell Carcinomas (Trunk)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	152	5.9	0.76 (0.52,1.11)	0.134
Medium	161	2.5		
High	164	3.1		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
	Analysis Results for Log_2 (Initial Dioxin)[c]		
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
475	0.86 (0.57,1.28)	0.439	AGE (p=0.047) LAT (p=0.061) ASB (p<0.001)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-9. (Continued)
Analysis of Basal Cell Carcinomas (Trunk)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,002	2.8		
Background RH	356	3.1	1.16 (0.57,2.38)	0.676
Low RH	232	4.7	1.64 (0.80,3.36)	0.176
High RH	245	2.9	0.99 (0.42,2.30)	0.977
Low plus High RH	477	3.8	1.31 (0.71,2.40)	0.389

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	982			DXCAT*INS (p=0.038) AGE (p=0.020) EYE (p=0.122) SUN2HR (p=0.060) SUNRPT (p=0.044) LAT (p=0.013) ASB (p=0.012) HERB (p=0.036)
Background RH	354	0.67 (0.30,1.49)**	0.324**	
Low RH	228	1.08 (0.48,2.45)**	0.851**	
High RH	244	0.74 (0.29,1.91)**	0.530**	
Low plus High RH	472	0.92 (0.45,1.88)**	0.818**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table F-2-5 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 10-9. (Continued)
Analysis of Basal Cell Carcinomas (Trunk)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	3.2 (281)	4.4 (272)	2.9 (280)	0.97 (0.77,1.23)	0.801
5	3.5 (285)	4.9 (268)	2.1 (280)	0.97 (0.78,1.20)	0.780
6[c]	3.5 (284)	4.9 (268)	2.1 (280)	0.95 (0.74,1.23)	0.714

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	829	1.09 (0.83,1.43)**	0.551**	CURR*INS (p=0.032) AGE (p=0.002) SUNRPT (p=0.141) ASB (p=0.002)
5	833	1.05 (0.82,1.33)**	0.713**	CURR*INS (p=0.024) AGE (p<0.001) ASB (p=0.001)
6[d]	832	1.07 (0.83,1.38)**	0.613**	CURR*INS (p=0.021) AGE (p<0.001) ASB (p=0.001)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table F-2-5 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 10-10.
Analysis of Basal Cell Carcinomas (Upper Extremities)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***886***	***1.9***	***1.15 (0.60,2.21)***	***0.796***
	Comparison	***1,198***	***1.7***		
Officer	Ranch Hand	357	3.6	1.39 (0.64,3.03)	0.534
	Comparison	490	2.7		
Enlisted Flyer	Ranch Hand	150	0.7	1.25 (0.08,20.13)	0.999
	Comparison	187	0.5		
Enlisted Groundcrew	Ranch Hand	379	0.8	0.69 (0.17,2.76)	0.844
	Comparison	521	1.2		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.16 (0.60,2.24)***	***0.662***	AGE (p=0.023)
Officer	1.32 (0.60,2.91)	0.489	EYE (p=0.134)
Enlisted Flyer	1.36 (0.08,22.19)	0.829	SUNRPT (p=0.022)
Enlisted Groundcrew	0.71 (0.17,2.89)	0.633	LAT (p=0.119) ASB (p=0.094)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 10-10. (Continued)
Analysis of Basal Cell Carcinomas (Upper Extremities)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	152	1.3	0.59 (0.31,1.13)	0.082
Medium	161	3.1		
High	164	0.0		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
	Analysis Results for Log_2 (Initial Dioxin)[c]		
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
477	0.57 (0.29,1.14)	0.081	EYE (p=0.030) ASB (p=0.050) IONRAD (p=0.092)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-10. (Continued)
Analysis of Basal Cell Carcinomas (Upper Extremities)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,002	1.8		
Background RH	356	2.3	1.41 (0.60,3.32)	0.428
Low RH	232	1.7	0.89 (0.30,2.66)	0.829
High RH	245	1.2	0.62 (0.18,2.14)	0.449
Low plus High RH	477	1.5	0.75 (0.31,1.82)	0.523

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	983			AGE (p=0.088) EYE (p=0.105) SUNRPT (p=0.055) LAT (p=0.093) ASB (p=0.060)
Background RH	354	1.30 (0.55,3.09)	0.549	
Low RH	228	0.87 (0.29,2.66)	0.810	
High RH	244	0.73 (0.21,2.59)	0.625	
Low plus High RH	472	0.81 (0.33,1.98)	0.638	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 10-10. (Continued)
Analysis of Basal Cell Carcinomas (Upper Extremities)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Yes/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	2.5 (281)	1.5 (272)	1.4 (280)	0.82 (0.56,1.18)	0.271
5	2.1 (285)	2.6 (268)	0.7 (280)	0.87 (0.65,1.16)	0.340
6[c]	2.1 (284)	2.6 (268)	0.7 (280)	0.86 (0.63,1.18)	0.360

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	n	Analysis Results for Log_2 (Current Dioxin + 1) Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	833	0.88 (0.59,1.32)	0.538	AGE (p=0.115) EYE (p=0.007)
5	833	0.93 (0.68,1.27)	0.643	AGE (p=0.104) EYE (p=0.007)
6[d]	832	0.92 (0.64,1.30)	0.620	AGE (p=0.107) EYE (p=0.007)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Covariate adjustment retained age, eye color, reaction of skin to sun after repeated exposure, average lifetime residential latitude, and asbestos exposure in the final adjusted model.

The Model 2 relative risk estimates resulting from the unadjusted and adjusted analyses of basal cell carcinomas of the upper extremities were marginally significant and less than one, indicating an inverse relationship (Table 10-10(c,d): $p=0.082$, Est. RR=0.59 and $p=0.081$, Adj. RR=0.57). Eye color, asbestos exposure, and ionizing radiation exposure were significant in the final adjusted model. All unadjusted and adjusted contrasts examined from Model 3 were nonsignificant (Table 10-10(e,f): $p>0.42$ for all contrasts). Significant covariates in the final model include age, eye color, reaction of skin to sun after repeated exposure, average lifetime residential latitude, and asbestos exposure.

Paralleling Model 3 analysis, the unadjusted and adjusted analyses of basal cell carcinomas on the upper extremities displayed nonsignificant results for Models 4, 5, and 6 (Table 10-10(g,h): $p>0.27$ for all analyses). Each model adjusted for age and eye color in the final model.

Basal Cell Carcinomas (Lower Extremities)

Each contrast examined from the Model 1 analysis of basal cell carcinomas on the lower extremities was nonsignificant (Table 10-11(a,b): $p>0.83$ for all contrasts). Differences between Ranch Hands and Comparisons within the enlisted flyer and groundcrew occupations were not conducted because of the sparse number of participants with a history of a basal cell carcinoma on the lower extremities. Adjusted analyses were not performed for Model 1 or any of the other five models because of the sparse number of participants with a basal cell carcinoma on the lower extremities.

No Ranch Hands were found to have a history of a basal cell carcinoma on the lower extremities in Model 2 analyses. The Model 3 unadjusted analysis contrast between Ranch Hands in the background category and Comparisons was examined and found to be nonsignificant (Table 10-11(e): $p=0.596$).

Unadjusted analysis of basal cell carcinomas on the lower extremities exhibited nonsignificant results for each of Models 4, 5, and 6 (Table 10-11(g): $p>0.18$ for each model).

Squamous Cell Carcinomas

All examinations of differences between Ranch Hands and Comparisons were nonsignificant for the Model 1 analysis of squamous cell carcinomas (Table 10-12(a,b): $p>0.13$ for all contrasts). Adjusted analysis retained age, reaction of skin to sun after repeated exposure, average lifetime residential latitude, and herbicide exposure in the final model.

Each unadjusted and adjusted analysis of squamous cell carcinomas for Models 2 and 3 was nonsignificant (Table 10-12(c-f): $p>0.14$ for all analyses). Model 2 adjusted for

Table 10-11.
Analysis of Basal Cell Carcinomas (Lower Extremities)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***886***	***0.1***	***0.45 (0.05,4.33)***	***0.839***
	Comparison	***1,198***	***0.3***		
Officer	Ranch Hand	357	0.3	1.37 (0.09,22.03)	0.999
	Comparison	490	0.2		
Enlisted Flyer	Ranch Hand	150	0.0	--	--
	Comparison	187	0.0		
Enlisted Groundcrew	Ranch Hand	379	0.0	--	--
	Comparison	521	0.4		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks**
All	--	--	
Officer	--	--	
Enlisted Flyer	--	--	
Enlisted Groundcrew	--	--	

--: Adjusted analysis not performed due to the sparse number of abnormalities.

Table 10-11. (Continued)
Analysis of Basal Cell Carcinomas (Lower Extremities)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)	p-Value
Low	152	0.0	--	--
Medium	161	0.0		
High	164	0.0		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)			
n	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
--	--	--	

--: Unadjusted and adjusted analyses not performed due to zero abnormalities.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-11. (Continued)
Analysis of Basal Cell Carcinomas (Lower Extremities)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,002	0.2		
Background RH	356	0.3	1.95 (0.17,22.90)	0.596
Low RH	232	0.0	--	--
High RH	245	0.0	--	--
Low plus High RH	477	0.0	--	--

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Comparison	--			
Background RH	--	--	--	
Low RH	--	--	--	
High RH	--	--	--	
Low plus High RH	--	--	--	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

--: Adjusted analysis not performed due to the sparse number of abnormalities.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 10-11. (Continued)
Analysis of Basal Cell Carcinomas (Lower Extremities)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.4 (281)	0.0 (272)	0.0 (280)	0.60 (0.13,2.74)	0.491
5	0.0 (285)	0.4 (268)	0.0 (280)	1.06 (0.34,3.32)	0.923
6[c]	0.0 (284)	0.4 (268)	0.0 (280)	0.34 (0.07,1.74)	0.188

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
4	--	--	--	
5	--	--	--	
6	--	--	--	

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

--: Adjusted analysis not performed due to the sparse number of abnormalities.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 10-12.
Analysis of Squamous Cell Carcinomas

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***886***	***1.4***	***1.16 (0.53,2.52)***	***0.859***
	Comparison	***1,198***	***1.2***		
Officer	Ranch Hand	357	1.7	0.91 (0.32,2.59)	0.999
	Comparison	490	1.8		
Enlisted Flyer	Ranch Hand	150	1.3	1.25 (0.17,8.98)	0.999
	Comparison	187	1.1		
Enlisted Groundcrew	Ranch Hand	379	1.1	1.84 (0.41,8.28)	0.671
	Comparison	521	0.6		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.92 (0.69,5.35)***	***0.208***	AGE ($p<0.001$)
Officer	1.44 (0.42,4.99)	0.564	SUNRPT ($p=0.146$)
Enlisted Flyer	2.13 (0.26,17.61)	0.483	LAT ($p=0.120$)
Enlisted Groundcrew	3.47 (0.67,18.00)	0.138	HERB ($p=0.122$)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 10-12. (Continued)
Analysis of Squamous Cell Carcinomas

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	152	1.3	0.85 (0.43,1.70)	0.641
Medium	161	1.2		
High	164	1.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
472	0.78 (0.36,1.68)	0.512	SUNRPT (p=0.014) LAT (p=0.103) ASB (p=0.040)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-12. (Continued)
Analysis of Squamous Cell Carcinomas

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,002	1.1		
Background RH	356	1.7	1.59 (0.58,4.40)	0.367
Low RH	232	1.7	1.54 (0.49,4.92)	0.461
High RH	245	0.8	0.73 (0.16,3.32)	0.680
Low plus High RH	477	1.3	1.12 (0.41,3.07)	0.820

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,002			AGE (p=0.001) HERB (p=0.103)
Background RH	356	2.54 (0.72,8.95)	0.146	
Low RH	232	2.57 (0.63,10.52)	0.189	
High RH	245	1.68 (0.31,9.18)	0.551	
Low plus High RH	477	2.17 (0.61,7.73)	0.231	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 10-12. (Continued)
Analysis of Squamous Cell Carcinomas

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Yes/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	1.4 (281)	2.2 (272)	0.7 (280)	0.91 (0.61,1.35)	0.628
5	1.4 (285)	2.2 (268)	0.7 (280)	0.97 (0.69,1.35)	0.834
6[c]	1.4 (284)	2.2 (268)	0.7 (280)	0.89 (0.62,1.28)	0.539

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	n	Analysis Results for Log_2 (Current Dioxin + 1) Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	833	0.98 (0.64,1.50)	0.921	AGE (p=0.095) IONRAD (p=0.128)
5	833	1.03 (0.72,1.48)	0.864	AGE (p=0.086) IONRAD (p=0.125)
6[d]	828	1.01 (0.69,1.46)	0.970	AGE (p=0.080) SUNRPT (p=0.149) IONRAD (p=0.131)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

reaction of skin to sun after repeated exposure, average lifetime residential latitude, and asbestos exposure. Model 3 retained age and herbicide exposure in the final adjusted model.

Associations between squamous cell carcinomas and current dioxin were nonsignificant for all analyses of Models 4, 5, and 6 (Table 10-12(g,h): $p>0.53$ for all analyses). Age and ionizing radiation were retained in each adjusted model. Model 6 also adjusted for reaction of skin to sun after repeated exposure.

Nonmelanomas

The Model 1 analysis of nonmelanomas showed no significant differences between Ranch Hands and Comparisons for both the unadjusted and adjusted analyses (Table 10-13(a,b): $p>0.28$ for all analyses). Age, reaction of skin to sun after at least 2 hours, reaction of skin to sun after repeated exposure, and average lifetime residential latitude were retained in the final adjusted model.

A significant association between nonmelanomas and initial dioxin resulted from the unadjusted and adjusted analyses of Model 2, where the history of a nonmelanoma decreased as initial dioxin measurements increased (Table 10-13(c): $p=0.007$, Est. $RR=0.74$ and $p=0.032$, Adj. $RR=0.76$). The adjusted results were based on the final adjusted model after deletion of a significant current dioxin-by-insecticide exposure interaction. Analyses stratified by each level of insecticide exposure are presented in Appendix Table F-2-6. Other significant covariates were age, reaction of skin to sun after at least 2 hours, reaction of skin to sun after repeated exposure, and average lifetime residential latitude.

The Model 3 unadjusted contrast of Ranch Hands in the high dioxin category versus Comparisons showed marginally significant results (Table 10-13(e): $p=0.064$, Est. $RR=0.61$). Of Ranch Hands in the high dioxin category, 7.4 percent had a history of a nonmelanoma, whereas 11.1 percent of Comparisons showed a history of a nonmelanoma. Of Ranch Hands in the low dioxin category, 16.4 percent showed a history of a nonmelanoma, and the contrast with Comparisons was significant (Table 10-13(e): $p=0.042$, Est. $RR=1.52$). Results were marginally significant for the adjusted contrast between Ranch Hands in the low category and Comparisons (Table 10-13(f): $p=0.078$, Adj. $RR=1.47$). All other contrasts were nonsignificant (Table 10-13(e,f): $p>0.13$ for all remaining contrasts). Age, reaction of skin to sun after at least 2 hours, reaction of skin to sun after repeated exposure, average lifetime residential latitude, and insecticide exposure were significant in the Model 3 adjusted analysis.

Significant associations between current dioxin levels and nonmelanomas were found from the unadjusted analysis of Models 4 and 6 (Table 10-13(g,h): $p=0.034$, Est. $RR=0.86$ and $p=0.016$, Est. $RR=0.85$). A history of a nonmelanoma decreased as current dioxin levels increased. The Model 5 analyses were nonsignificant, as were the adjusted analyses of Models 4 and 6 (Table 10-13(g,h): $p>0.13$ for all remaining analyses). Each model adjusted for the covariate effects of age, reaction of skin to sun after at least 2 hours exposure, reaction of skin to sun after repeated exposure, and average lifetime residential latitude. Model 6 also retained ionizing radiation exposure.

Table 10-13.
Analysis of Nonmelanomas

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***886***	***12.6***	***1.14 (0.87,1.49)***	***0.374***
	Comparison	***1,198***	***11.3***		
Officer	Ranch Hand	357	17.1	1.22 (0.84,1.77)	0.351
	Comparison	490	14.5		
Enlisted Flyer	Ranch Hand	150	14.7	1.23 (0.65,2.30)	0.636
	Comparison	187	12.3		
Enlisted Groundcrew	Ranch Hand	379	7.7	0.97 (0.59,1.59)	0.999
	Comparison	521	7.9		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.17 (0.88,1.54)***	***0.282***	AGE ($p<0.001$)
Officer	1.22 (0.83,1.80)	0.310	SUN2HR ($p<0.001$)
Enlisted Flyer	1.30 (0.68,2.49)	0.430	SUNRPT ($p=0.001$)
Enlisted Groundcrew	1.00 (0.60,1.66)	0.997	LAT ($p<0.001$)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 10-13. (Continued)
Analysis of Nonmelanomas

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	152	15.8	0.74 (0.58,0.93)	0.007
Medium	161	12.4		
High	164	7.3		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
472	0.76 (0.59,0.99)**	0.032**	INIT*INS (p=0.026) AGE (p=0.119) SUN2HR (p=0.050) SUNRPT (p=0.034) LAT (p=0.010)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table F-2-6 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-13. (Continued)
Analysis of Nonmelanomas

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,002	11.1		
Background RH	356	13.5	1.32 (0.92,1.91)	0.134
Low RH	232	16.4	1.52 (1.02,2.27)	0.042
High RH	245	7.4	0.61 (0.36,1.03)	0.064
Low plus High RH	477	11.7	1.03 (0.73,1.45)	0.869

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	984			AGE ($p<0.001$) SUN2HR ($p=0.001$) SUNRPT ($p=0.003$) LAT ($p<0.001$) INS ($p=0.134$)
Background RH	354	1.19 (0.81,1.75)	0.366	
Low RH	228	1.47 (0.96,2.24)	0.078	
High RH	244	0.74 (0.43,1.28)	0.283	
Low plus High RH	472	1.11 (0.77,1.59)	0.570	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 10-13. (Continued)
Analysis of Nonmelanomas

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Yes/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	13.9 (281)	15.1 (272)	8.6 (280)	0.86 (0.74,0.99)	0.034
5	13.3 (285)	14.9 (268)	9.3 (280)	0.91 (0.81,1.03)	0.131
6[c]	13.4 (284)	14.9 (268)	9.3 (280)	0.85 (0.75,0.97)	0.016

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	n	Analysis Results for Log_2 (Current Dioxin + 1) Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	826	0.93 (0.79,1.08)	0.319	AGE ($p<0.001$) SUN2HR ($p=0.046$) SUNRPT ($p=0.041$) LAT ($p=0.030$)
5	826	0.98 (0.86,1.11)	0.692	AGE ($p<0.001$) SUN2HR ($p=0.045$) SUNRPT ($p=0.037$) LAT ($p=0.032$)
6[d]	825	0.91 (0.79,1.04)	0.176	AGE ($p<0.001$) SUN2HR ($p=0.025$) SUNRPT ($p=0.046$) LAT ($p=0.025$) IONRAD ($p=0.128$)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Melanomas

The Model 1 analysis of melanomas was nonsignificant for each unadjusted and adjusted contrast analyzed (Table 10-14(a,b): $p > 0.46$ for each contrast). Differences between Ranch Hands and Comparisons within the enlisted flyer occupation were not considered because of the absence of melanoma within this cohort. Average lifetime residential latitude, industrial chemical exposure, and degreasing chemical exposure were significant in the final adjusted model.

The unadjusted test of association between initial dioxin and melanomas for Model 2 yielded nonsignificant results (Table 10-14(c): $p=0.136$, Est. RR=0.61). However, after covariate adjustment, a significant inverse relationship was revealed (Table 10-14(d): $p=0.021$, Adj. RR=0.43). Skin color, hair color, industrial chemical exposure, and degreasing chemical exposure were significant covariates. From the unadjusted analysis of Model 3, a marginally significant difference was found between Ranch Hands in the low dioxin category and Comparisons (Table 10-14(e): $p=0.076$, Est. RR=2.79). All other unadjusted and adjusted contrasts were nonsignificant (Table 10-14(e,f): $p > 0.14$ for all remaining contrasts). Significant covariates in Model 3 were average lifetime residential latitude, industrial chemical exposure, and degreasing chemical exposure.

For Models 4, 5, and 6, all unadjusted and adjusted results from the analysis of melanomas were nonsignificant (Table 10-14(g,h): $p > 0.86$ for all analyses). Each adjusted analysis retained hair color, average lifetime residential latitude, industrial chemical exposure, and degreasing chemical exposure in the final adjusted model.

After the analyses were well underway, an error in the classification of one participant's race was discovered. He was listed in the data base as Black, when he was actually non-Black. The participant was a 50-year-old Comparison, and he was a member of the enlisted flyer cohort, with a current serum dioxin value < 10 ppt. Because the participant is a Comparison, he was only included in the Model 1 and Model 3 analyses (see Chapter 7, Statistical Methods). This participant had a melanoma and was excluded from the analyses of melanomas, because he was erroneously coded as Black. Additional analyses of melanomas were performed with this participant properly coded as non-Black. Results from this analysis did not indicate any change in conclusions based on this misclassification. The additional analyses are shown in Appendix Table F-1-2.

Systemic Neoplasms

Each unadjusted and adjusted systemic neoplasms analysis examined using Models 1 through 6 was nonsignificant (Table 10-15: $p > 0.13$ for all contrasts). Age and industrial chemical exposure were significant in each of the final adjusted models.

Malignant Systemic Neoplasms

The Model 1 analyses of a history of a malignant systemic neoplasm revealed that differences between Ranch Hands and Comparisons were nonsignificant (Table 10-16(a,b):

Table 10-14.
Analysis of Melanomas

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***886***	***1.2***	***1.49 (0.63,3.53)***	***0.486***
	Comparison	***1,198***	***0.8***		
Officer	Ranch Hand	357	1.7	1.66 (0.50,5.48)	0.596
	Comparison	490	1.0		
Enlisted Flyer	Ranch Hand	150	0.0	--	--
	Comparison	187	0.0		
Enlisted Groundcrew	Ranch Hand	379	1.3	1.38 (0.40,4.80)	0.852
	Comparison	521	1.0		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.37 (0.58,3.26)***	***0.474***	LAT (p=0.062) IC (p=0.013) DC (p=0.040)
Officer	1.57 (0.47,5.21)	0.465	
Enlisted Flyer	--	--	
Enlisted Groundcrew	1.24 (0.35,4.35)	0.740	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

--: Adjusted relative risk, confidence interval, and p-value not presented due to zero abnormalities.

Table 10-14. (Continued)
Analysis of Melanomas

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	152	2.0	0.61 (0.30,1.24)	0.136
Medium	161	1.2		
High	164	1.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
477	0.43 (0.19,0.99)	0.021	SKIN (p=0.047) HAIR (p=0.003) IC (p=0.013) DC (p=0.008)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-14. (Continued)
Analysis of Melanomas

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,002	0.8		
Background RH	356	0.8	1.05 (0.27,4.01)	0.948
Low RH	232	2.2	2.79 (0.90,8.66)	0.076
High RH	245	0.8	1.01 (0.21,4.84)	0.987
Low plus High RH	477	1.5	1.86 (0.67,5.21)	0.235

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	991			LAT (p=0.033) IC (p=0.048) DC (p=0.053)
Background RH	355	0.97 (0.25,3.76)	0.964	
Low RH	230	2.34 (0.74,7.40)	0.148	
High RH	245	0.93 (0.19,4.53)	0.930	
Low plus High RH	475	1.64 (0.58,4.63)	0.351	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 10-14. (Continued)
Analysis of Melanomas

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Yes/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.7 (281)	2.2 (272)	0.7 (280)	0.98 (0.64,1.50)	0.934
5	1.1 (285)	1.1 (268)	1.4 (280)	0.99 (0.69,1.42)	0.944
6[c]	1.1 (284)	1.1 (268)	1.4 (280)	1.02 (0.69,1.51)	0.938

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	830	1.01 (0.64,1.57)	0.982	HAIR (p=0.086) LAT (p=0.019) IC (p=0.130) DC (p=0.044)
5	830	1.01 (0.69,1.48)	0.950	HAIR (p=0.087) LAT (p=0.019) IC (p=0.130) DC (p=0.043)
6[d]	829	1.03 (0.69,1.54)	0.869	HAIR (p=0.088) LAT (p=0.020) IC (p=0.135) DC (p=0.044)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 10-15.
Analysis of Systemic Neoplasms

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***943***	***21.1***	***1.04 (0.85,1.28)***	***0.755***
	Comparison	***1,280***	***20.5***		
Officer	Ranch Hand	361	21.3	0.91 (0.66,1.27)	0.640
	Comparison	502	22.9		
Enlisted Flyer	Ranch Hand	160	24.4	1.13 (0.69,1.85)	0.712
	Comparison	203	22.2		
Enlisted Groundcrew	Ranch Hand	422	19.7	1.14 (0.82,1.57)	0.489
	Comparison	575	17.7		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.03 (0.84,1.27)***	***0.772***	AGE ($p<0.001$) IC ($p=0.086$)
Officer	0.90 (0.64,1.25)	0.520	
Enlisted Flyer	1.13 (0.69,1.85)	0.640	
Enlisted Groundcrew	1.13 (0.82,1.57)	0.459	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 10-15. (Continued)
Analysis of Systemic Neoplasms

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	170	23.5	0.93 (0.79,1.09)	0.354
Medium	172	23.3		
High	172	18.6		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
514	1.01 (0.86,1.20)	0.876	AGE (p=0.004) IC (p=0.057)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-15. (Continued)
Analysis of Systemic Neoplasms

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	20.7		
Background RH	372	19.6	0.98 (0.72,1.32)	0.873
Low RH	255	23.9	1.17 (0.85,1.62)	0.340
High RH	259	19.7	0.91 (0.65,1.28)	0.594
Low plus High RH	514	21.8	1.04 (0.80,1.34)	0.784

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,062			AGE ($p<0.001$) IC ($p=0.043$)
Background RH	372	0.89 (0.65,1.20)	0.437	
Low RH	255	1.12 (0.80,1.55)	0.513	
High RH	259	1.08 (0.76,1.53)	0.671	
Low plus High RH	514	1.10 (0.85,1.43)	0.481	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 10-15. (Continued)
Analysis of Systemic Neoplasms

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Yes/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	18.4 (293)	24.0 (296)	20.2 (297)	1.02 (0.91,1.14)	0.746
5	19.1 (298)	22.3 (292)	21.3 (296)	1.02 (0.93,1.12)	0.668
6[c]	19.2 (297)	22.3 (292)	21.3 (296)	1.01 (0.91,1.12)	0.875

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	n	Analysis Results for Log_2 (Current Dioxin + 1) Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	886	1.10 (0.97,1.23)	0.130	AGE ($p<0.001$) IC ($p=0.037$)
5	886	1.08 (0.98,1.20)	0.135	AGE ($p<0.001$) IC ($p=0.037$)
6[d]	885	1.08 (0.97,1.20)	0.185	AGE ($p<0.001$) IC ($p=0.039$)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

$p \geq 0.34$ for all contrasts). Adjusted analysis retained age and lifetime cigarette smoking history in the final adjusted model.

The association between malignant systemic neoplasms and initial dioxin was significant in the Model 2 unadjusted analysis. A history of a malignant systemic neoplasm decreased among Ranch Hands as initial dioxin levels increased (Table 10-16(c): $p=0.004$, Est. $RR=0.63$). Age and the initial dioxin-by-lifetime cigarette smoking history interaction were significant in the final adjusted model. Appendix Table F-2-7 presents results stratified by levels of lifetime cigarette smoking history. A marginally significant association between initial dioxin and malignant systemic neoplasms was found among Ranch Hands with no lifetime cigarette smoking history (Appendix Table F-2-7(a): $p=0.081$, Adj. $RR=0.29$).

The Model 3 unadjusted analysis revealed that Ranch Hands in the low dioxin category exhibited a significantly greater history of a malignant systemic neoplasm than Comparisons (Table 10-16(e): $p=0.024$, Est. $RR=1.87$). The analogous adjusted contrast was marginally significant (Table 10-16(f): $p=0.060$, Adj. $RR=1.72$). All remaining contrasts were nonsignificant (Table 10-16(e,f): $p \geq 0.22$ for all remaining contrasts). Adjusted results accounted for the covariates age and lifetime cigarette smoking history.

Associations between malignant systemic neoplasms and current dioxin were found to be nonsignificant from the unadjusted and adjusted analyses of Models 4, 5, and 6 (Table 10-16(g,h): $p > 0.35$ for all analyses). Model 4 adjusted results are based on the final model after deletion of the significant current dioxin-by-degreasing chemical exposure interaction. Model 5 and 6 adjusted results are based on the final model after deletion of the significant current dioxin-by-lifetime cigarette smoking history and current dioxin-by-degreasing chemical exposure interactions. Results stratified by each level of degreasing chemical exposure for Models 4, 5, and 6, and lifetime cigarette smoking history for Models 5 and 6, are presented in Appendix F-2-7. Age was significant in each model, and Model 4 also adjusted for lifetime cigarette smoking history.

Benign Systemic Neoplasms

All differences in the history of a benign systemic neoplasm between Ranch Hands and Comparisons were nonsignificant (Table 10-17(a,b): $p \geq 0.24$ for all contrasts). Age and industrial chemical exposure were significant in the final model.

Results from the Model 2 and 3 analyses of benign systemic neoplasms were similar to Model 1. All associations between benign systemic neoplasms and initial dioxin and categorized dioxin were nonsignificant (Table 10-17(c-f): $p > 0.46$ for all analyses). Model 2 was adjusted for lifetime alcohol history and industrial chemical exposure and Model 3 was adjusted for age and industrial chemical exposure.

The analysis of the relationship between benign systemic neoplasms and current dioxin was nonsignificant for Models 4, 5, and 6 (Table 10-17(g,h): $p > 0.71$ for all analyses). Lifetime alcohol history and industrial chemical exposure were significant covariates in each adjusted final model.

Table 10-16.
Analysis of Malignant Systemic Neoplasms

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***943***	***5.0***	***1.17 (0.78,1.74)***	***0.507***
	Comparison	***1,280***	***4.3***		
Officer	Ranch Hand	361	6.1	0.95 (0.54,1.67)	0.980
	Comparison	502	6.4		
Enlisted Flyer	Ranch Hand	160	8.1	1.54 (0.67,3.54)	0.414
	Comparison	203	5.4		
Enlisted Groundcrew	Ranch Hand	422	2.8	1.37 (0.61,3.09)	0.575
	Comparison	575	2.1		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.16 (0.77,1.75)***	***0.479***	AGE ($p<0.001$) PACKYR ($p=0.051$)
Officer	0.94 (0.53,1.66)	0.820	
Enlisted Flyer	1.51 (0.65,3.52)	0.340	
Enlisted Groundcrew	1.37 (0.60,3.14)	0.454	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 10-16. (Continued)
Analysis of Malignant Systemic Neoplasms

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	170	7.1	0.63 (0.44,0.89)	0.004
Medium	172	8.1		
High	172	1.7		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
514	****	****	INIT*PACKYR (p=0.008) AGE (p<0.001)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

**** Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.01$); adjusted relative risk, confidence interval, and p-value not presented; refer to Appendix Table F-2-7 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-16. (Continued)
Analysis of Malignant Systemic Neoplasms

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	4.2		
Background RH	372	4.0	1.03 (0.57,1.89)	0.914
Low RH	255	8.2	1.87 (1.09,3.22)	0.024
High RH	259	3.1	0.67 (0.31,1.45)	0.309
Low plus High RH	514	5.6	1.26 (0.77,2.04)	0.356

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,060			AGE ($p<0.001$) PACKYR ($p=0.066$)
Background RH	371	0.94 (0.51,1.73)	0.834	
Low RH	255	1.72 (0.98,3.01)	0.060	
High RH	259	0.90 (0.41,1.99)	0.801	
Low plus High RH	514	1.37 (0.83,2.26)	0.220	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 10-16. (Continued)
Analysis of Malignant Systemic Neoplasms

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Yes/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	3.8 (293)	8.1 (296)	3.0 (297)	0.94 (0.76,1.17)	0.585
5	4.7 (298)	5.5 (292)	4.7 (296)	0.99 (0.82,1.18)	0.872
6[c]	4.7 (297)	5.5 (292)	4.7 (296)	0.95 (0.78,1.15)	0.585

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	n	Analysis Results for Log_2 (Current Dioxin + 1) Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	885	1.06 (0.85,1.37)**	0.537**	CURR*DC (p=0.024) AGE (p<0.001) PACKYR (p=0.069)
5	885	1.10 (0.90,1.35)**	0.359**	CURR*PACKYR (p=0.039) CURR*DC (p=0.036) AGE (p<0.001)
6[d]	884	1.08 (0.87,1.34)**	0.506**	CURR*PACKYR (p=0.038) CURR*DC (p=0.035) AGE (p<0.001)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table F-2-7 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 10-17.
Analysis of Benign Systemic Neoplasms

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***943***	***16.4***	***1.07 (0.85,1.34)***	***0.611***
	Comparison	***1,280***	***15.6***		
Officer	Ranch Hand	361	14.1	0.86 (0.59,1.25)	0.476
	Comparison	502	16.1		
Enlisted Flyer	Ranch Hand	160	19.4	1.15 (0.68,1.97)	0.699
	Comparison	203	17.2		
Enlisted Groundcrew	Ranch Hand	422	17.3	1.24 (0.88,1.75)	0.254
	Comparison	575	14.4		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.06 (0.84,1.34)***	***0.607***	AGE ($p<0.001$) IC ($p=0.075$)
Officer	0.84 (0.58,1.24)	0.384	
Enlisted Flyer	1.15 (0.67,1.98)	0.602	
Enlisted Groundcrew	1.23 (0.87,1.74)	0.240	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 10-17. (Continued)
Analysis of Benign Systemic Neoplasms

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	170	16.5	1.02 (0.86,1.22)	0.804
Medium	172	16.3		
High	172	16.3		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
	Analysis Results for Log_2 (Initial Dioxin)[c]		
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
502	1.00 (0.83,1.20)	0.989	DRKYR (p=0.124) IC (p=0.018)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-17. (Continued)
Analysis of Benign Systemic Neoplasms

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	15.6		
Background RH	372	16.1	1.07 (0.77,1.48)	0.689
Low RH	255	16.5	1.05 (0.73,1.52)	0.795
High RH	259	16.2	1.02 (0.71,1.48)	0.911
Low plus High RH	514	16.3	1.04 (0.78,1.38)	0.812

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,062			AGE ($p<0.001$) IC ($p=0.057$)
Background RH	372	0.99 (0.72,1.38)	0.976	
Low RH	255	1.02 (0.70,1.48)	0.931	
High RH	259	1.15 (0.79,1.68)	0.464	
Low plus High RH	514	1.08 (0.81,1.44)	0.605	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 10-17. (Continued)
Analysis of Benign Systemic Neoplasms

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Yes/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	15.0 (293)	16.6 (296)	17.2 (297)	1.02 (0.91,1.16)	0.712
5	15.4 (298)	16.8 (292)	16.6 (296)	1.01 (0.91,1.12)	0.829
6[c]	15.5 (297)	16.8 (292)	16.6 (296)	1.02 (0.91,1.14)	0.765

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	867	1.01 (0.89,1.15)	0.841	DRKYR (p=0.059) IC (p=0.010)
5	867	1.00 (0.90,1.12)	0.940	DRKYR (p=0.058) IC (p=0.011)
6[d]	866	1.01 (0.90,1.14)	0.870	DRKYR (p=0.057) IC (p=0.011)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Systemic Neoplasms of Uncertain Behavior or Unspecified Nature

All Ranch Hand versus Comparison contrasts examined from the Model 1 analysis of systemic neoplasms of uncertain behavior or unspecified nature were nonsignificant (Table 10-18(a,b): $p > 0.59$ for all contrasts). Contrasts within the enlisted flyer cohort were not performed because no Ranch Hand enlisted flyers exhibited a history of a systemic neoplasm of uncertain behavior or unspecified nature. Age was significant in the adjusted model.

All unadjusted and adjusted results also were nonsignificant from each Model 2 and 3 analysis of systemic neoplasms of uncertain behavior or unspecified nature (Table 10-18(c-f): $p > 0.44$ for all analyses). No covariates were significant in Model 2, although age was significant in Model 3.

The analyses of systemic neoplasms of uncertain behavior or unspecified nature from Models 4, 5, and 6 were comparable to the above analyses. All unadjusted and adjusted results were nonsignificant (Table 10-18(g,h): $p > 0.25$ for all analyses). Each Model 4, 5, and 6 adjusted analysis retained age and the current dioxin-by-asbestos exposure interaction in the final model. All adjusted results presented in Table 10-18(h) are based upon deletion of the interaction from the final model. For each model, Appendix Table F-2-8 displays results stratified for each level of asbestos exposure.

Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck)

Differences in the history of a malignant systemic neoplasm of the eye, ear, face, head, or neck were examined between Ranch Hands and Comparisons in the analysis of Model 1. All unadjusted and adjusted contrasts were nonsignificant (Table 10-19(a,b): $p > 0.26$ for all contrasts). The adjusted analysis retained age and lifetime cigarette smoking history in the final model.

The unadjusted analysis of malignant systemic neoplasms of the eye, ear, face, head, or neck from Model 2 was nonsignificant (Table 10-19(c): $p = 0.182$). Adjusted analysis included degreasing chemical exposure and an initial dioxin-by-lifetime cigarette smoking history interaction in the final model. No significant results were found in analyses of malignant systemic neoplasms of the eye, ear, face, head, or neck stratified by lifetime cigarette smoking history (Appendix Table F-2-9(a)).

Each Model 3 contrast was nonsignificant (Table 10-19(e,f): $p > 0.16$ for all unadjusted and adjusted contrasts). Adjusted analyses revealed a significant categorized dioxin-by-lifetime cigarette smoking history interaction and a categorized dioxin-by-degreasing chemical exposure interaction. Model 3 also adjusted for age, ionizing radiation exposure, and industrial chemical exposure. Results stratified by levels of lifetime cigarette smoking and levels of degreasing chemical exposure are presented in Appendix Table F-2-9. Adjusted results were based on the final model after deletion of the significant interactions.

Model 4, 5, and 6 analyses of malignant systemic neoplasms of the eye, ear, face, head, or neck revealed nonsignificant associations with current dioxin (Table 10-19(g,h): $p > 0.48$

Table 10-18.
Analysis of Systemic Neoplasms of Uncertain Behavior or Unspecified Nature

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***943***	***1.6***	***0.92 (0.48,1.79)***	***0.948***
	Comparison	***1,280***	***1.7***		
Officer	Ranch Hand	361	2.8	1.27 (0.53,3.03)	0.749
	Comparison	502	2.2		
Enlisted Flyer	Ranch Hand	160	0.0	--	--
	Comparison	203	1.0		
Enlisted Groundcrew	Ranch Hand	422	1.2	0.75 (0.25,2.27)	0.817
	Comparison	575	1.6		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***0.92 (0.47,1.78)***	***0.803***	AGE (p=0.010)
Officer	1.26 (0.53,3.01)	0.599	
Enlisted Flyer	--	--	
Enlisted Groundcrew	0.75 (0.25,2.27)	0.616	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

--: Adjusted relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Table 10-18. (Continued)
Analysis of Systemic Neoplasms of Uncertain Behavior or Unspecified Nature

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	170	2.4	0.91 (0.54,1.52)	0.709
Medium	172	1.2		
High	172	1.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[a]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
514	0.91 (0.54,1.52)	0.709	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-18. (Continued)
Analysis of Systemic Neoplasms of Uncertain Behavior or Unspecified Nature

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	1.8		
Background RH	372	1.6	0.94 (0.37,2.38)	0.890
Low RH	255	2.0	1.08 (0.40,2.94)	0.877
High RH	259	1.2	0.62 (0.18,2.13)	0.448
Low plus High RH	514	1.6	0.85 (0.37,1.96)	0.698

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,062			AGE (p=0.028)
Background RH	372	0.88 (0.34,2.24)	0.785	
Low RH	255	1.03 (0.38,2.80)	0.957	
High RH	259	0.72 (0.21,2.48)	0.599	
Low plus High RH	514	0.89 (0.38,2.05)	0.776	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 10-18. (Continued)
Analysis of Systemic Neoplasms of Uncertain Behavior or Unspecified Nature

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Yes/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	2.1 (293)	1.4 (296)	1.4 (297)	0.88 (0.60,1.28)	0.487
5	1.7 (298)	2.1 (292)	1.0 (296)	0.88 (0.65,1.19)	0.404
6[c]	1.7 (297)	2.1 (292)	1.0 (296)	0.83 (0.60,1.14)	0.255

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	886	0.92 (0.62,1.37)**	0.689**	CURR*ASB (p=0.009) AGE (p=0.101)
5	886	0.91 (0.66,1.25)**	0.552**	CURR*ASB (p=0.015) AGE (p=0.099)
6[d]	885	0.86 (0.61,1.21)**	0.389**	CURR*ASB (p=0.015) AGE (p=0.112)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table F-2-8 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 10-19.
Analysis of Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***943***	***1.1***	***1.36 (0.56,3.28)***	***0.644***
	Comparison	***1,280***	***0.8***		
Officer	Ranch Hand	361	1.4	2.34 (0.56,9.84)	0.406
	Comparison	502	0.6		
Enlisted Flyer	Ranch Hand	160	1.3	0.63 (0.11,3.48)	0.905
	Comparison	203	2.0		
Enlisted Groundcrew	Ranch Hand	422	0.7	1.37 (0.27,6.80)	0.999
	Comparison	575	0.5		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.34 (0.55,3.24)***	***0.519***	AGE (p=0.035) PACKYR (p=0.104)
Officer	2.28 (0.54,9.62)	0.263	
Enlisted Flyer	0.61 (0.11,3.37)	0.571	
Enlisted Groundcrew	1.37 (0.27,6.79)	0.703	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 10-19. (Continued)
Analysis of Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	170	2.4	0.65 (0.32,1.30)	0.182
Medium	172	0.0		
High	172	1.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
	Analysis Results for Log_2 (Initial Dioxin)[c]		
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
514	****	****	INIT*PACKYR (p=0.003) DC (p=0.015)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

**** Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.01$); adjusted relative risk, confidence interval, and p-value not presented; refer to Appendix Table F-2-9 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-19. (Continued)
Analysis of Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	0.6		
Background RH	372	0.8	1.57 (0.38,6.39)	0.532
Low RH	255	1.6	2.49 (0.69,8.98)	0.163
High RH	259	0.8	1.21 (0.24,6.17)	0.820
Low plus High RH	514	1.2	1.85 (0.58,5.86)	0.295

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,060			DXCAT*PACKYR (p=0.030) DXCAT*DC (p=0.028) AGE (p=0.032) IONRAD (p=0.010) IC (p=0.081)
Background RH	371	1.43 (0.34,5.98)**	0.623**	
Low RH	255	2.32 (0.62,8.63)**	0.210**	
High RH	259	1.86 (0.36,9.71)**	0.460**	
Low plus High RH	514	2.14 (0.66,6.90)**	0.202**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interactions ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table F-2-9 for further analysis of these interactions.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 10-19. (Continued)
Analysis of Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Yes/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.7 (293)	1.7 (296)	0.7 (297)	0.99 (0.63,1.56)	0.976
5	1.0 (298)	1.4 (292)	0.7 (296)	0.97 (0.66,1.42)	0.855
6[c]	1.0 (297)	1.4 (292)	0.7 (296)	1.06 (0.70,1.61)	0.793

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	886	1.11 (0.70,1.75)	0.672	DC (p=0.062)
5	886	1.05 (0.71,1.58)	0.795	DC (p=0.068)
6[d]	885	1.17 (0.76,1.81)	0.489	DC (p=0.066)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

for all unadjusted and adjusted analyses). Each adjusted model retained degreasing chemical exposure.

Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx)

All unadjusted and adjusted contrasts examined from the Model 1 analysis of malignant systemic neoplasms of the oral cavity, pharynx, or larynx were nonsignificant (Table 10-20(a,b): $p > 0.72$ for all contrasts). Age and ionizing radiation exposure were significant covariates in the final adjusted model.

The Model 2 and 3 analyses of malignant systemic neoplasms of the oral cavity, pharynx, or larynx also were nonsignificant for the unadjusted and adjusted models (Table 10-20(c-f): $p > 0.27$ for all analyses). Significant covariates for Model 2 were lifetime cigarette smoking history, industrial chemical exposure, and herbicide exposure. Model 3 adjusted for age and ionizing radiation exposure.

Unadjusted results from the Model 4, 5, and 6 analyses of malignant systemic neoplasms of the oral cavity, pharynx, or larynx were each nonsignificant (Table 10-20(g): $p > 0.21$ for each unadjusted analysis). Adjusted analysis of Models 4, 5, and 6 each revealed marginally significant associations with current dioxin (Table 10-20(h): $p=0.076$, Adj. RR=1.79; $p=0.070$; Adj. RR=1.72; and $p=0.087$, Adj. RR=1.73 respectively). Each adjusted model retained ionizing radiation exposure, industrial chemical exposure, and herbicide exposure in the final model.

Malignant Systemic Neoplasms (Esophagus)

Because of the sparse number of participants with a history of a malignant systemic neoplasm of the esophagus, statistical analysis was not performed. Frequencies and associated percentages for a history of a malignant systemic neoplasm of the esophagus are presented for each model in Table 10-21.

Malignant Systemic Neoplasms (Brain)

Because of the sparse number of participants with a history of a malignant systemic neoplasm of the brain, only the unadjusted analysis of all Ranch Hands versus all Comparisons was performed for Model 1. The results of this analysis displayed a nonsignificant difference between groups (Table 10-22(a): $p=0.999$).

Of Models 2 through 6, only unadjusted analyses of malignant systemic neoplasms of the brain were possible for Models 4 and 5 and yielded nonsignificant results (Table 10-22(g): $p > 0.41$ for each model). No other analyses were performed because of the sparse number of participants with a history of a malignant systemic neoplasm of the brain. Table 10-22(c,e,g) displays frequencies and associated percentages of the history of a malignant systemic neoplasm of the brain for each of these models.

Table 10-20.
Analysis of Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***943***	***0.4***	***0.91 (0.26,3.21)***	***0.999***
	Comparison	***1,280***	***0.5***		
Officer	Ranch Hand	361	0.3	0.69 (0.06,7.69)	0.999
	Comparison	502	0.4		
Enlisted Flyer	Ranch Hand	160	1.3	1.27 (0.18,9.13)	0.999
	Comparison	203	1.0		
Enlisted Groundcrew	Ranch Hand	422	0.2	0.68 (0.06,7.53)	0.999
	Comparison	575	0.4		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.00 (0.28,3.58)***	***0.995***	AGE (p=0.008) IONRAD (p=0.132)
Officer	0.77 (0.07,8.57)	0.828	
Enlisted Flyer	1.42 (0.20,10.30)	0.727	
Enlisted Groundcrew	0.72 (0.06,8.06)	0.791	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 10-20. (Continued)
Analysis of Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	170	0.6	1.17 (0.52,2.62)	0.706
Medium	172	0.0		
High	172	1.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
514	1.50 (0.63,3.59)	0.356	PACKYR (p=0.106) IC (p=0.070) HERB (p=0.069)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-20. (Continued)
Analysis of Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	0.5		
Background RH	372	0.3	0.58 (0.07,5.08)	0.624
Low RH	255	0.4	0.77 (0.09,6.65)	0.810
High RH	259	0.8	1.55 (0.29,8.26)	0.605
Low plus High RH	514	0.6	1.15 (0.27,4.94)	0.847

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,062			AGE (p=0.003) IONRAD (p=0.081)
Background RH	372	0.62 (0.07,5.55)	0.673	
Low RH	255	0.77 (0.09,6.84)	0.811	
High RH	259	2.57 (0.47,14.00)	0.275	
Low plus High RH	514	1.44 (0.33,6.32)	0.626	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 10-20. (Continued)
Analysis of Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.0 (293)	0.7 (296)	0.7 (297)	1.47 (0.80,2.69)	0.229
5	0.0 (298)	0.7 (292)	0.7 (296)	1.43 (0.82,2.50)	0.213
6[c]	0.0 (297)	0.7 (292)	0.7 (296)	1.43 (0.79,2.59)	0.251

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	886	1.79 (0.96,3.33)	0.076	IONRAD (p=0.093) IC (p=0.054) HERB (p=0.107)
5	886	1.72 (0.96,3.09)	0.070	IONRAD (p=0.091) IC (p=0.054) HERB (p=0.116)
6[d]	885	1.73 (0.94,3.19)	0.087	IONRAD (p=0.091) IC (p=0.054) HERB (p=0.119)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 10-21.
Analysis of Malignant Systemic Neoplasms (Esophagus)

a) MODEL 1: RANCH HANDS VS. COMPARISONS			
Occupational Category	**Group**	**n**	**Percent Yes**
All	***Ranch Hand***	***943***	***0.0***
	Comparison	***1,280***	***0.1***
Officer	Ranch Hand	361	0.0
	Comparison	502	0.0
Enlisted Flyer	Ranch Hand	160	0.0
	Comparison	203	0.5
Enlisted Groundcrew	Ranch Hand	422	0.0
	Comparison	575	0.0

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN		
Initial Dioxin Category Summary Statistics		
Initial Dioxin	**n**	**Percent Yes**
Low	170	0.0
Medium	172	0.0
High	172	0.0

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-21. (Continued)
Analysis of Malignant Systemic Neoplasms (Esophagus)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY		
Dioxin Category	n	Percent Yes
Comparison	1,062	0.1
Background RH	372	0.0
Low RH	255	0.0
High RH	259	0.0
Low plus High RH	514	0.0

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.

d) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN			
	Current Dioxin Category Percent Yes/(n)		
Model[a]	Low	Medium	High
4	0.0 (293)	0.0 (296)	0.0 (297)
5	0.0 (298)	0.0 (292)	0.0 (296)
6	0.0 (297)	0.0 (292)	0.0 (296)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 10-22.
Analysis of Malignant Systemic Neoplasms (Brain)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***943***	***0.1***	***1.35 (0.09,21.74)***	***0.999***
	Comparison	***1,280***	***0.1***		
Officer	Ranch Hand	361	0.3	--	--
	Comparison	502	0.0		
Enlisted Flyer	Ranch Hand	160	0.0	--	--
	Comparison	203	0.5		
Enlisted Groundcrew	Ranch Hand	422	0.0	--	--
	Comparison	575	0.0		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks**
All	--	--	
Officer	--	--	
Enlisted Flyer	--	--	
Enlisted Groundcrew	--	--	

--: Estimated relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Table 10-22. (Continued)
Analysis of Malignant Systemic Neoplasms (Brain)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)**	
Initial Dioxin	**n**	**Percent Yes**	**Estimated Relative Risk (95% C.I.)**	**p-Value**
Low	170	0.6	--	--
Medium	172	0.0		
High	172	0.0		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)			
n	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks**
--	--	--	

--: Estimated relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-22. (Continued)
Analysis of Malignant Systemic Neoplasms (Brain)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
Comparison	1,062	0.0		
Background RH	372	0.0	--	--
Low RH	255	0.4	--	--
High RH	259	0.0	--	--
Low plus High RH	514	0.2	--	--

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Comparison	--			
Background RH	--	--	--	
Low RH	--	--	--	
High RH	--	--	--	
Low plus High RH	--	--	--	

--: Estimated relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$10 ppt.
Low (Ranch Hand): Current Dioxin $>$10 ppt, 10 ppt $<$ Initial Dioxin $\leq$143 ppt.
High (Ranch Hand): Current Dioxin $>$10 ppt, Initial Dioxin $>$143 ppt.

Table 10-22. (Continued)
Analysis of Malignant Systemic Neoplasms (Brain)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.0 (293)	0.3 (296)	0.0 (297)	0.78 (0.18,3.33)	0.726
5	0.3 (298)	0.0 (292)	0.0 (296)	0.66 (0.26,1.64)	0.416
6	0.3 (297)	0.0 (292)	0.0 (296)	--	--

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
4	--	--	--	
5	--	--	--	
6	--	--	--	

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

--: Estimated relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum)

Because of the sparse number of participants with a history of a malignant systemic neoplasm of the thymus, heart, or mediastinum, statistical analysis was not performed for Models 1, 2, and 3. Table 10-23(a,c,e) displays frequencies and associated percentages of a history of a malignant systemic neoplasm of the thymus, heart, or mediastinum for each model.

Analyses performed for Models 4, 5, and 6 revealed nonsignificant associations between malignant systemic neoplasms of the thymus, heart, or mediastinum and current dioxin (Table 10-23(g,h): $p > 0.21$ for all analyses). Each model adjusted for lifetime alcohol history, and Model 6 also adjusted for lifetime cigarette smoking history.

Malignant Systemic Neoplasms (Thyroid Gland)

Over all occupations and within the officer occupation, results from the unadjusted analysis of malignant systemic neoplasms of the thyroid gland indicated no significant differences between the two groups (Table 10-24(a): $p > 0.77$ for both contrasts). Because of the sparse number of participants with a history of a malignant systemic neoplasm of the thyroid gland, only the candidate covariates of age, lifetime cigarette smoking history, and lifetime alcohol history were considered. Each covariate was found to be nonsignificant, and consequently adjusted results are identical to the unadjusted results (Table 10-24(b)). Analysis was not conducted within the enlisted flyer and enlisted groundcrew occupational cohorts because of the sparse number of participants with a history of a malignant systemic neoplasm of the thyroid gland within these strata.

A significant inverse association between initial dioxin and malignant systemic neoplasms of the thyroid gland was found from the unadjusted and adjusted analyses of Model 2 (Table 10-24(c,d): $p=0.044$, Est. $RR=0.14$ and $p=0.041$, Adj. $RR=0.13$ respectively). A history of a malignant systemic neoplasm of the thyroid gland decreased as initial dioxin measurements increased. Lifetime cigarette smoking history exhibited a significant effect in the final adjusted model.

The Model 3 analysis was not performed because of the sparse number of participants with a history of a malignant systemic neoplasm of the thyroid gland. Table 10-24(e) displays frequencies and associated percentages of a history of a malignant systemic neoplasm of the thyroid gland.

Each unadjusted and adjusted analysis of malignant systemic neoplasms of the thyroid gland from Models 4, 5, and 6 produced nonsignificant results (Table 10-24(g,h): $p > 0.77$ for all analyses). Lifetime cigarette smoking history was a significant covariate in each adjusted model.

Malignant Systemic Neoplasms (Bronchus and Lung)

All unadjusted and adjusted contrasts examined from the Model 1 analysis of malignant systemic neoplasms of the bronchus or lung were nonsignificant (Table 10-25(a,b): $p \geq 0.13$

Table 10-23.
Analysis of Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***943***	***0.2***	--	--
	Comparison	***1,280***	***0.0***		
Officer	Ranch Hand	361	0.3	--	--
	Comparison	502	0.0		
Enlisted Flyer	Ranch Hand	160	0.0	--	--
	Comparison	203	0.0		
Enlisted Groundcrew	Ranch Hand	422	0.2	--	--
	Comparison	575	0.0		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
All	--	--	
Officer	--	--	
Enlisted Flyer	--	--	
Enlisted Groundcrew	--	--	

--: Estimated relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Table 10-23. (Continued)
Analysis of Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)**	
Initial Dioxin	**n**	**Percent Yes**	**Estimated Relative Risk (95% C.I.)**	**p-Value**
Low	170	0.0	--	--
Medium	172	0.0		
High	172	0.0		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)			
n	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks**
--	--	--	

--: Estimated relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-23. (Continued)
Analysis of Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
Comparison	1,062	0.0		
Background RH	372	0.3	--	--
Low RH	255	0.0	--	--
High RH	259	0.0	--	--
Low plus High RH	514	0.0	--	--

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Comparison	--			
Background RH	--	--	--	
Low RH	--	--	--	
High RH	--	--	--	
Low plus High RH	--	--	--	

--: Estimated relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$10 ppt.
Low (Ranch Hand): Current Dioxin $>$10 ppt, 10 ppt $<$ Initial Dioxin $\leq$143 ppt.
High (Ranch Hand): Current Dioxin $>$10 ppt, Initial Dioxin $>$143 ppt.

Table 10-23. (Continued)
Analysis of Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Yes/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.3 (293)	0.0 (296)	0.0 (297)	0.43 (0.10,1.91)	0.271
5	0.3 (298)	0.0 (292)	0.0 (296)	0.58 (0.26,1.31)	0.259
6[c]	0.3 (297)	0.0 (292)	0.0 (296)	0.63 (0.22,1.81)	0.449

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	867	0.40 (0.08,2.03)	0.232	DRKYR (p=0.111)
5	867	0.53 (0.21,1.33)	0.216	DRKYR (p=0.108)
6[d]	866	0.61 (0.18,2.09)	0.448	PACKYR (p=0.105) DRKYR (p=0.045)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 10-24.
Analysis of Malignant Systemic Neoplasms (Thyroid Gland)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***943***	***0.2***	***1.36 (0.19.9.66)***	***0.999***
	Comparison	***1,280***	***0.2***		
Officer	Ranch Hand	361	0.6	2.80 (0.25,30.90)	0.774
	Comparison	502	0.2		
Enlisted Flyer	Ranch Hand	160	0.0	--	--
	Comparison	203	0.0		
Enlisted Groundcrew	Ranch Hand	422	0.0	--	--
	Comparison	575	0.2		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
All	***1.36 (0.19,9.66)***	***0.999***	
Officer	2.80 (0.25,30.90)	0.774	
Enlisted Flyer	--	--	
Enlisted Groundcrew	--	--	

--: Estimated relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Table 10-24. (Continued)
Analysis of Malignant Systemic Neoplasms (Thyroid Gland)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	170	1.2	0.14 (0.01,2.34)	0.044
Medium	172	0.0		
High	172	0.0		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
514	0.13 (0.01,2.16)	0.044	PACKYR (p=0.041)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-24. (Continued)
Analysis of Malignant Systemic Neoplasms (Thyroid Gland)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
Comparison	1,062	0.0		
Background RH	372	0.0	--	--
Low RH	255	0.8	--	--
High RH	259	0.0	--	--
Low plus High RH	514	0.4	--	--

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Comparison	--			
Background RH	--	--	--	
Low RH	--	--	--	
High RH	--	--	--	
Low plus High RH	--	--	--	

--: Estimated relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$10 ppt.
Low (Ranch Hand): Current Dioxin $>$10 ppt, 10 ppt $<$ Initial Dioxin $\leq$143 ppt.
High (Ranch Hand): Current Dioxin $>$10 ppt, Initial Dioxin $>$143 ppt.

Table 10-24. (Continued)
Analysis of Malignant Systemic Neoplasms (Thyroid Gland)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.0 (293)	0.7 (296)	0.0 (297)	0.88 (0.32,2.37)	0.789
5	0.0 (298)	0.7 (292)	0.0 (296)	0.90 (0.40,2.01)	0.796
6[c]	0.0 (297)	0.7 (292)	0.0 (296)	0.95 (0.39,2.28)	0.902

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	885	0.87 (0.32,2.36)	0.774	PACKYR (p=0.043)
5	885	0.90 (0.38,2.11)	0.804	PACKYR (p=0.043)
6[d]	884	0.91 (0.37,2.25)	0.843	PACKYR (p=0.047)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 10-25.
Analysis of Malignant Systemic Neoplasms (Bronchus and Lung)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***943***	***0.6***	***2.04 (0.58,7.26)***	***0.420***
	Comparison	***1,280***	***0.3***		
Officer	Ranch Hand	361	1.1	5.61 (0.63,50.43)	0.200
	Comparison	502	0.2		
Enlisted Flyer	Ranch Hand	160	0.6	0.63 (0.06,7.03)	0.999
	Comparison	203	1.0		
Enlisted Groundcrew	Ranch Hand	422	0.2	1.36 (0.09,21.86)	0.999
	Comparison	575	0.2		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.95 (0.54,7.04)***	***0.301***	AGE (p=0.003) PACKYR (p=0.022)
Officer	5.53 (0.60,50.64)	0.130	
Enlisted Flyer	0.62 (0.05,7.02)	0.700	
Enlisted Groundcrew	1.18 (0.07,20.41)	0.911	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 10-25. (Continued)
Analysis of Malignant Systemic Neoplasms (Bronchus and Lung)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	170	0.6	0.61 (0.23,1.63)	0.275
Medium	172	1.2		
High	172	0.0		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
502	0.44 (0.13,1.46)	0.120	PACKYR (p=0.132) DRKYR (p=0.024)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-25. (Continued)
Analysis of Malignant Systemic Neoplasms (Bronchus and Lung)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	0.4		
Background RH	372	0.8	2.40 (0.51,11.28)	0.268
Low RH	255	1.2	2.48 (0.53,11.59)	0.249
High RH	259	0.0	--	--
Low plus High RH	514	0.6	1.06 (0.21,5.27)	0.944

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,060			AGE (p=0.064) PACKYR (p=0.142)
Background RH	371	2.37 (0.48,11.64)	0.286	
Low RH	255	2.15 (0.42,10.93)	0.357	
High RH	259	--	--	
Low plus High RH	514	1.20 (0.24,5.98)	0.828	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

--: Adjusted relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$10 ppt.
Low (Ranch Hand): Current Dioxin $>$10 ppt, 10 ppt $<$ Initial Dioxin $\leq$143 ppt.
High (Ranch Hand): Current Dioxin $>$10 ppt, Initial Dioxin $>$143 ppt.

Table 10-25. (Continued)
Analysis of Malignant Systemic Neoplasms (Bronchus and Lung)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Yes/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.7 (293)	1.4 (296)	0.0 (297)	0.80 (0.45,1.45)	0.460
5	1.0 (298)	0.7 (292)	0.3 (296)	0.92 (0.57,1.47)	0.719
6[c]	1.0 (297)	0.7 (292)	0.3 (296)	0.80 (0.48,1.31)	0.378

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	n	Analysis Results for Log_2 (Current Dioxin + 1) Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	867	0.97 (0.54,1.75)	0.906	AGE (p=0.065) PACKYR (p=0.039) DRKYR (p=0.135)
5	867	1.06 (0.66,1.70)	0.817	AGE (p=0.055) PACKYR (p=0.035) DRKYR (p=0.126)
6[d]	884	0.89 (0.53,1.49)	0.668	AGE (p=0.110) PACKYR (p=0.103)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

for all contrasts). Significant covariates included in the final model were age and lifetime cigarette smoking history.

Similar to Model 1, unadjusted and adjusted analyses of malignant systemic neoplasms of the bronchus or lung from Models 2 and 3 yielded nonsignificant results (Table 10-25(c-f): $p \geq 0.12$ for both analyses). Model 2 adjusted for lifetime cigarette smoking history and lifetime alcohol history. Age and lifetime cigarette smoking history were significant covariates for Model 3. The Model 3 contrast between Ranch Hands categorized with high current dioxin levels and Comparisons was not examined because no participants with a history of a malignant systemic neoplasm of the bronchus or lung were within the high Ranch Hand category.

All unadjusted and adjusted analyses of malignant systemic neoplasms of the bronchus or lung from Models 4, 5, and 6 were nonsignificant (Table 10-25(g,h): $p > 0.37$ for each analysis). Significant covariates from each adjusted model were age and lifetime cigarette smoking history. Lifetime alcohol history also was significant for Models 4 and 5.

Malignant Systemic Neoplasms (Colon and Rectum)

All results from the unadjusted and adjusted analysis of malignant systemic neoplasms of the colon or rectum for Model 1 were nonsignificant (Table 10-26(a,b): $p > 0.43$ for all contrasts performed). Contrasts for the enlisted flyer and enlisted groundcrew strata were not examined because of the sparse number of participants with a history of a malignant systemic neoplasm of the colon or rectum within these strata. Age was retained in the final model.

Both the unadjusted and adjusted analyses of malignant systemic neoplasms of the colon or rectum for Model 2 were nonsignificant (Table 10-26(c,d): $p > 0.24$ for both analyses). Age, lifetime cigarette smoking history, and ionizing radiation exhibited significant covariate effects in the final adjusted model. Model 3 unadjusted analysis revealed a significant difference between Comparisons and Ranch Hands in the low dioxin category (Table 10-26(e): $p = 0.034$, Est. $RR = 5.12$). Because no covariates were significant in the final adjusted model, adjusted results are identical to the unadjusted results. The Model 3 contrast between Ranch Hands in the high dioxin category and Comparisons was not examined because no Ranch Hands with a history of a malignant systemic neoplasm of the colon or rectum were in the high dioxin category.

All associations examined between malignant systemic neoplasms of the colon or rectum and current dioxin from Models 4, 5, and 6 were nonsignificant (Table 10-26(g,h): $p \geq 0.25$ for all analyses). Each model adjusted for age, lifetime cigarette smoking history, and insecticide exposure.

Malignant Systemic Neoplasms (Kidney and Bladder)

Differences in a history of a malignant systemic neoplasm of the kidney or bladder among Ranch Hands and Comparisons were examined in Model 1 analyses. Over all occupations and within the officer occupation, differences were nonsignificant for both the

Table 10-26.
Analysis of Malignant Systemic Neoplasms (Colon and Rectum)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***943***	***0.5***	***1.70 (0.46,6.35)***	***0.645***
	Comparison	***1,280***	***0.3***		
Officer	Ranch Hand	361	0.8	1.39 (0.28,6.95)	0.999
	Comparison	502	0.6		
Enlisted Flyer	Ranch Hand	160	1.3	--	--
	Comparison	203	0.0		
Enlisted Groundcrew	Ranch Hand	422	0.0	--	--
	Comparison	575	0.2		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.69 (0.45,6.33)***	***0.432***	AGE (p=0.144)
Officer	1.38 (0.28,6.91)	0.692	
Enlisted Flyer	--	--	
Enlisted Groundcrew	--	--	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

--: Relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Table 10-26. (Continued)
Analysis of Malignant Systemic Neoplasms (Colon and Rectum)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	170	0.6	0.61 (0.24,1.55)	0.245
Medium	172	1.7		
High	172	0.0		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
514	0.70 (0.22,2.26)	0.525	AGE (p=0.042) PACKYR (p=0.076) IONRAD (p=0.047)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-26. (Continued)
Analysis of Malignant Systemic Neoplasms (Colon and Rectum)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	0.3		
Background RH	372	0.3	1.14 (0.12,11.07)	0.910
Low RH	255	1.6	5.12 (1.13,23.27)	0.034
High RH	259	0.0	--	--
Low plus High RH	514	0.8	2.48 (0.55,11.23)	0.239

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ab]	p-Value	Covariate Remarks
Comparison	1,062			
Background RH	372	1.14 (0.12,11.07)	0.910	
Low RH	255	5.12 (1.13,23.27)	0.034	
High RH	259	--	--	
Low plus High RH	514	2.48 (0.55,11.23)	0.239	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

--: Relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.

Table 10-26. (Continued)
Analysis of Malignant Systemic Neoplasms (Colon and Rectum)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.3 (293)	1.0 (296)	0.3 (297)	1.03 (0.57,1.87)	0.923
5	0.3 (298)	0.0 (292)	1.4 (296)	1.14 (0.68,1.90)	0.628
6[c]	0.3 (297)	0.0 (292)	1.4 (296)	0.97 (0.55,1.72)	0.919

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	885	1.34 (0.65,2.73)	0.440	AGE (p=0.003) PACKYR (p=0.107) INS (p=0.065)
5	885	1.44 (0.78,2.65)	0.250	AGE (p=0.002) PACKYR (p=0.099) INS (p=0.067)
6[d]	884	1.21 (0.61,2.43)	0.589	AGE (p=0.002) PACKYR (p=0.108) INS (p=0.099)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

unadjusted and adjusted analyses (Table 10-27(a,b): $p > 0.26$ for all contrasts examined). Contrasts within the enlisted flyer and enlisted groundcrew strata were not examined because of the sparse number of participants with a history of a malignant systemic neoplasm of the kidney or bladder within these strata. Adjusted analysis retained age, lifetime cigarette smoking history, and insecticide exposure in the final model.

The unadjusted and adjusted results from the Model 2 and 3 analyses of malignant systemic neoplasms of the kidney or bladder were nonsignificant (Table 10-27(c,d): $p > 0.12$ for all analyses). Significant covariates in Model 2 were race, lifetime cigarette smoking history, industrial chemical exposure, insecticide exposure, and herbicide exposure. Model 3 adjusted for age, lifetime cigarette smoking history, ionizing radiation exposure, and insecticide exposure.

Similar to Models 1, 2, and 3, each Model 4, 5, and 6 analysis of malignant systemic neoplasms of the kidney or bladder was nonsignificant (Table 10-27(g,h): $p > 0.73$ for all analyses). Models 4, 5, and 6 each adjusted for lifetime cigarette smoking history, ionizing radiation exposure, and insecticide exposure. Model 6 also adjusted for race.

Malignant Systemic Neoplasms (Prostate)

All results from the analysis of malignant systemic neoplasms of the prostate were nonsignificant (Table 10-28(a-h): $p > 0.14$ for all analyses). Each model adjusted for age, and Model 2 also adjusted for degreasing chemical exposure. Herbicide exposure was significant in Model 3. In addition to age, Models 3, 4, 5, and 6 also adjusted for the dioxin-by-degreasing chemical exposure interaction. Adjusted results seen in Table 10-28(h) for Models 4 through 6 are based on the final model after the deletion of the significant interaction. Appendix Table F-2-10 displays relative risk estimates for each level of the dioxin-by-degreasing chemical interaction for Models 3 through 6.

Malignant Systemic Neoplasms (Testicles)

Analysis of malignant systemic neoplasms of the testicles was performed for Models 2, 4, 5, and 6, and the results of each analysis were nonsignificant (Table 10-29(c,d,g,h): $p > 0.35$ for each analysis). Because of the sparse number of participants with a history of a malignant systemic neoplasm of the testicles, only the candidate covariates of age, lifetime cigarette smoking history, and lifetime alcohol history were considered. Lifetime alcohol history and lifetime cigarette smoking history were significant for the final adjusted Models 2, 4, and 5. Model 6 adjusted for lifetime cigarette smoking history only.

The sparse number of participants with a history of a malignant systemic neoplasm of the testicles precluded analyses of Models 1 and 3. However, there were three Ranch Hands and zero Comparisons with a history of a malignant systemic neoplasm of the testicles.

Malignant Systemic Neoplasms (Ill-Defined Sites)

The Model 1 overall contrast between Ranch Hands and Comparisons was nonsignificant for both the unadjusted and adjusted analyses of a history of a malignant

Table 10-27.
Analysis of Malignant Systemic Neoplasms (Kidney and Bladder)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***943***	***0.6***	***1.63 (0.50,5.37)***	***0.610***
	Comparison	***1,280***	***0.4***		
Officer	Ranch Hand	361	0.8	0.83 (0.20,3.51)	0.999
	Comparison	502	1.0		
Enlisted Flyer	Ranch Hand	160	0.6	--	--
	Comparison	203	0.0		
Enlisted Groundcrew	Ranch Hand	422	0.5	--	--
	Comparison	575	0.0		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***2.00 (0.58,6.89)***	***0.268***	AGE (p=0.009)
Officer	0.89 (0.20,3.92)	0.881	PACKYR (p=0.006)
Enlisted Flyer	--	--	INS (p=0.016)
Enlisted Groundcrew	--	--	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

--: Adjusted relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Table 10-27. (Continued)
Analysis of Malignant Systemic Neoplasms (Kidney and Bladder)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	170	0.6	0.68 (0.28,1.65)	0.359
Medium	172	1.7		
High	172	0.0		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
514	0.66 (0.21,2.10)	0.455	RACE (p=0.100) PACKYR (p=0.019) IC (p=0.107) INS (p=0.095) HERB (p=0.141)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-27. (Continued)
Analysis of Malignant Systemic Neoplasms (Kidney and Bladder)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	0.4		
Background RH	372	0.5	1.47 (0.26,8.19)	0.261
Low RH	255	1.2	3.01 (0.66,13.61)	0.154
High RH	259	0.4	1.00 (0.11,9.10)	0.997
Low plus High RH	514	0.8	2.01 (0.50,8.14)	0.328

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,060			AGE (p=0.030) PACKYR (p=0.009) IONRAD (p=0.101) INS (p=0.021)
Background RH	371	1.83 (0.31,10.94)	0.507	
Low RH	255	3.59 (0.70,18.42)	0.125	
High RH	259	2.01 (0.21,19.12)	0.545	
Low plus High RH	514	2.95 (0.67,12.98)	0.152	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.

Table 10-27. (Continued)
Analysis of Malignant Systemic Neoplasms (Kidney and Bladder)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Yes/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.7 (293)	1.0 (296)	0.3 (297)	0.98 (0.56,1.71)	0.941
5	0.7 (298)	0.7 (292)	0.7 (296)	1.03 (0.64,1.66)	0.895
6[c]	0.7 (297)	0.7 (292)	0.7 (296)	0.97 (0.58,1.62)	0.915

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	885	1.03 (0.58,1.82)	0.914	PACKYR (p=0.006) IONRAD (p=0.083) INS (p<0.001)
5	885	1.09 (0.67,1.77)	0.731	PACKYR (p=0.006) IONRAD (p=0.075) INS (p<0.001)
6[d]	884	0.99 (0.58,1.71)	0.978	RACE (p=0.121) PACKYR (p=0.004) IONRAD (p=0.047) INS (p<0.001)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 10-28.
Analysis of Malignant Systemic Neoplasms (Prostate)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***943***	***1.7***	***0.94 (0.50,1.80)***	***0.989***
	Comparison	***1,280***	***1.8***		
Officer	Ranch Hand	361	2.5	0.78 (0.34,1.78)	0.694
	Comparison	502	3.2		
Enlisted Flyer	Ranch Hand	160	2.5	1.28 (0.31,5.18)	0.999
	Comparison	203	2.0		
Enlisted Groundcrew	Ranch Hand	422	0.7	1.37 (0.27,6.80)	0.999
	Comparison	575	0.5		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***0.95 (0.49,1.84)***	***0.869***	AGE ($p<0.001$)
Officer	0.80 (0.34,1.87)	0.605	
Enlisted Flyer	1.24 (0.30,5.17)	0.775	
Enlisted Groundcrew	1.29 (0.25,6.67)	0.762	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 10-28. (Continued)
Analysis of Malignant Systemic Neoplasms (Prostate)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	170	2.4	0.68 (0.39,1.19)	0.147
Medium	172	2.9		
High	172	0.6		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
514	0.94 (0.51,1.74)	0.835	AGE ($p<0.001$) DC ($p=0.078$)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-28. (Continued)
Analysis of Malignant Systemic Neoplasms (Prostate)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	2.1		
Background RH	372	1.3	0.72 (0.27,1.92)	0.508
Low RH	255	2.4	1.04 (0.41,2.61)	0.934
High RH	259	1.5	0.68 (0.23,2.01)	0.487
Low plus High RH	514	2.0	0.86 (0.40,1.84)	0.697

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,062			DXCAT*DC (p=0.004) AGE (p<0.001) HERB (p=0.047)
Background RH	372	****	****	
Low RH	255	****	****	
High RH	259	****	****	
Low plus High RH	514	****	****	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

**** Categorized dioxin-by-covariate interaction ($p \leq 0.01$); adjusted relative risk, confidence interval, and p-value not presented; refer to Appendix Table F-2-10 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.

Table 10-28. (Continued)
Analysis of Malignant Systemic Neoplasms (Prostate)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Yes/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	1.0 (293)	2.7 (296)	1.4 (297)	0.93 (0.65,1.33)	0.697
5	1.3 (298)	1.7 (292)	2.0 (296)	0.99 (0.73,1.33)	0.928
6[c]	1.4 (297)	1.7 (292)	2.0 (296)	0.92 (0.67,1.28)	0.625

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	886	1.04 (0.68,1.58)**	0.862**	CURR*DC (p=0.015) AGE (p<0.001)
5	886	1.08 (0.76,1.55)**	0.662**	CURR*DC (p=0.019) AGE (p<0.001)
6[d]	885	1.02 (0.70,1.49)**	0.924**	CURR*DC (p=0.020) AGE (p<0.001)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table F-2-10 for further analysis of this interaction.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 10-29.
Analysis of Malignant Systemic Neoplasms (Testicles)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***943***	***0.3***	--	--
	Comparison	***1,280***	***0.0***		
Officer	Ranch Hand	361	0.3	--	--
	Comparison	502	0.0		
Enlisted Flyer	Ranch Hand	160	0.6	--	--
	Comparison	203	0.0		
Enlisted Groundcrew	Ranch Hand	422	0.2	--	--
	Comparison	575	0.0		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks**
All	--	--	
Officer	--	--	
Enlisted Flyer	--	--	
Enlisted Groundcrew	--	--	

--: Estimated relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormailities.

Table 10-29. (Continued)
Analysis of Malignant Systemic Neoplasms (Testicles)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	170	0.6	0.65 (0.22,1.95)	0.408
Medium	172	1.2		
High	172	0.0		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
	Analysis Results for Log_2 (Initial Dioxin)[c]		
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
502	0.61 (0.20,1.87)	0.353	DRKYR (p=0.094) PACKYR (p=0.053)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-29. (Continued)
Analysis of Malignant Systemic Neoplasms (Testicles)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
Comparison	1,062	0.0		
Background RH	372	0.0	--	--
Low RH	255	0.8	--	--
High RH	259	0.4	--	--
Low plus High RH	514	0.6	--	--

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Comparison	--			
Background RH	--	--	--	
Low RH	--	--	--	
High RH	--	--	--	
Low plus High RH	--	--	--	

--: Estimated relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormailities.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.

Table 10-29. (Continued)
Analysis of Malignant Systemic Neoplasms (Testicles)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Yes/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.0 (293)	0.7 (296)	0.3 (297)	1.20 (0.58,2.50)	0.636
5	0.0 (298)	0.3 (292)	0.7 (296)	1.32 (0.69,2.53)	0.409
6[c]	0.0 (297)	0.3 (292)	0.7 (296)	1.11 (0.54,2.31)	0.774

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	n	Analysis Results for Log_2 (Current Dioxin + 1) Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	867	1.24 (0.60,2.57)	0.532	PACKYR (p=0.119) DRKYR (p=0.054)
5	867	1.33 (0.69,2.57)	0.384	PACKYR (p=0.121) DRKYR (p=0.054)
6[d]	884	1.16 (0.57,2.36)	0.691	PACKYR (p=0.123)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

systemic neoplasm of ill-defined sites (Table 10-30(a,b): $p > 0.46$ for both contrasts). Age and lifetime alcohol history were significant covariates in the final adjusted model. No other analyses were performed due to the sparse number of study participants with a history of a malignant systemic neoplasm of ill-defined sites. Table 10-30 presents sample sizes and frequencies of histories of malignant systemic neoplasms (ill-defined sites) for Models 2-6.

Malignant Systemic Neoplasms (Connective and Other Soft Tissue)

Due to the sparse number of participants with a history of a malignant systemic neoplasm of connective and other soft tissue, no analyses were conducted. Table 10-31 presents sample sizes and frequencies of histories of malignant systemic neoplasms of connective and other soft tissue for each model. Of the two malignant systemic neoplasms of connective and other soft tissues, which were both found in Comparisons, only one was a soft tissue sarcoma.

Carcinomas in Situ of the Penis, Other, and Unspecified Sites

Analysis of carcinomas in situ of the penis, other, and unspecified sites was performed for Models 2, 4, 5, and 6 and for selected contrasts from Models 1 and 3. Results were nonsignificant for each model (Table 10-32(a-h): $p > 0.14$ for each analysis). The sparse number of participants with a history of a carcinoma in situ precluded complete unadjusted analysis and, consequently, adjusted analyses.

Hodgkin's Disease

Selected contrasts analyzing history of Hodgkin's disease were examined from Models 1 and 3 and all results were nonsignificant (Table 10-33(a,e): $p > 0.50$ for all analyses conducted). The sparse number of participants with a history of Hodgkin's disease precluded analysis with Model 2. Frequencies of histories of Hodgkin's disease are presented in Table 10-33(a,c,e) for each model.

Results from the unadjusted and adjusted analyses from Models 4, 5, and 6 were nonsignificant (Table 10-33(g,h): $p > 0.55$ for all analyses). Because of the sparse number of participants with a history of Hodgkin's disease, only the candidate covariates of age, lifetime cigarette smoking history, and lifetime alcohol history were considered in these models. Each model retained age and lifetime alcohol history.

Leukemia

Unadjusted analyses of a history of leukemia were performed where possible for Models 1 through 6. All results were nonsignificant for each model (Table 10-34(a-h): $p \geq 0.30$ for each analysis).

Non-Hodgkin's Lymphoma

Unadjusted analysis of a history of non-Hodgkin's lymphoma was performed where possible for Models 1 through 3. No significant results were found (Table 10-35(a-f):

Table 10-30.
Analysis of Malignant Systemic Neoplasms (Ill-Defined Sites)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***943***	***0.1***	***0.45 (0.05,4.35)***	***0.842***
	Comparison	***1,280***	***0.2***		
Officer	Ranch Hand	361	0.0	--	--
	Comparison	502	0.4		
Enlisted Flyer	Ranch Hand	160	0.6	--	--
	Comparison	203	0.0		
Enlisted Groundcrew	Ranch Hand	422	0.0	--	--
	Comparison	575	0.2		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***0.45 (0.05,4.37)***	***0.467***	AGE (p=0.116) DRKYR (p=0.146)
Officer	--	--	
Enlisted Flyer	--	--	
Enlisted Groundcrew	--	--	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

--: Relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Table 10-30. (Continued)
Analysis of Malignant Systemic Neoplasms (Ill-Defined Sites)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)	p-Value
Low	170	0.0	--	--
Medium	172	0.0		
High	172	0.0		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)			
n	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
--	--	--	

--: Analysis not performed due to zero abnormalities.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-30. (Continued)
Analysis of Malignant Systemic Neoplasms (Ill-Defined Sites)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
Comparison	1,062	0.2		
Background RH	372	0.0	--	--
Low RH	255	0.0	--	--
High RH	259	0.0	--	--
Low plus High RH	514	0.0	--	--

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Comparison	--			
Background RH	--	--	--	
Low RH	--	--	--	
High RH	--	--	--	
Low plus High RH	--	--	--	

--: Relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$10 ppt.
Low (Ranch Hand): Current Dioxin $>$10 ppt, 10 ppt $<$ Initial Dioxin $\leq$143 ppt.
High (Ranch Hand): Current Dioxin $>$10 ppt, Initial Dioxin $>$143 ppt.

Table 10-30. (Continued)
Analysis of Malignant Systemic Neoplasms (Ill-Defined Sites)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)	p-Value
4	0.0 (293)	0.0 (296)	0.0 (297)	--	--
5	0.0 (298)	0.0 (292)	0.0 (296)	--	--
6	0.0 (297)	0.0 (292)	0.0 (296)	--	--

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
4	--	--	--	
5	--	--	--	
6	--	--	--	

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

--: Analysis not performed due to zero abnormalities.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 10-31.
Analysis of Malignant Systemic Neoplasms (Connective and Other Soft Tissue)

a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	n	Percent Yes
All	***Ranch Hand***	***943***	***0.0***
	Comparison	***1,280***	***0.2***
Officer	Ranch Hand	361	0.0
	Comparison	502	0.2
Enlisted Flyer	Ranch Hand	160	0.0
	Comparison	203	0.0
Enlisted Groundcrew	Ranch Hand	422	0.0
	Comparison	575	0.2

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

Initial Dioxin Category Summary Statistics

Initial Dioxin	n	Percent Yes
Low	170	0.0
Medium	172	0.0
High	172	0.0

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-31. (Continued)
Analysis of Malignant Systemic Neoplasms (Connective and Other Soft Tissue)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY		
Dioxin Category	n	Percent Yes
Comparison	1,062	0.2
Background RH	372	0.0
Low RH	255	0.0
High RH	259	0.0
Low plus High RH	514	0.0

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.

d) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN			
	Current Dioxin Category Percent Yes/(n)		
Model[a]	Low	Medium	High
4	0.0 (293)	0.0 (296)	0.0 (297)
5	0.0 (298)	0.0 (292)	0.0 (296)
6	0.0 (297)	0.0 (292)	0.0 (296)

[a] Model 4: Log_2 lipid-adjusted (current dioxin + 1).
Model 5: Log_2 whole-weight (current dioxin + 1).
Model 6: Log_2 whole-weight (current dioxin + 1), adjusted for log_2 total lipids.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 10-32.
Analysis of Carcinomas in Situ of the Penis, Other, and Unspecified Sites

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***943***	***0.1***	***1.36 (0.09,21.74)***	***0.999***
	Comparison	***1,280***	***0.1***		
Officer	Ranch Hand	361	0.3	--	--
	Comparison	502	0.0		
Enlisted Flyer	Ranch Hand	160	0.0	--	--
	Comparison	203	0.0		
Enlisted Groundcrew	Ranch Hand	422	0.0	--	--
	Comparison	575	0.2		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks**
All	--	--	
Officer	--	--	
Enlisted Flyer	--	--	
Enlisted Groundcrew	--	--	

--: Estimated relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Table 10-32. (Continued)
Analysis of Carcinomas in Situ of the Penis, Other, and Unspecified Sites

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	170	0.6	0.11 (0.00,9.47)	0.144
Medium	172	0.0		
High	172	0.0		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)			
n	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks**
--	--	--	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

--: Adjusted analysis not performed due to the sparse number of abnormalities.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-32. (Continued)
Analysis of Carcinomas in Situ of the Penis, Other, and Unspecified Sites

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
Comparison	1,062	0.1		
Background RH	372	0.0	--	--
Low RH	255	0.4	4.22 (0.26,68.18)	0.311
High RH	259	0.0	--	--
Low plus High RH	514	0.2	2.05 (0.13,33.72)	0.617

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Comparison	--			
Background RH	--	--	--	
Low RH	--	--	--	
High RH	--	--	--	
Low plus High RH	--	--	--	

--: Estimated relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$10 ppt.
Low (Ranch Hand): Current Dioxin $>$10 ppt, 10 ppt $<$ Initial Dioxin $\leq$143 ppt.
High (Ranch Hand): Current Dioxin $>$10 ppt, Initial Dioxin $>$143 ppt.

Table 10-32. (Continued)
Analysis of Carcinomas in Situ of the Penis, Other, and Unspecified Sites

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.0 (293)	0.3 (296)	0.0 (297)	0.89 (0.22,3.60)	0.864
5	0.0 (298)	0.3 (292)	0.0 (296)	0.88 (0.28,2.73)	0.826
6[c]	0.0 (297)	0.3 (292)	0.0 (296)	0.99 (0.28,3.47)	0.991

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
4	--	--	--	
5	--	--	--	
6	--	--	--	

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

--: Adjusted analysis not performed due to the sparse number of abnormalities.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 10-33.
Analysis of Hodgkin's Disease

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***943***	***0.1***	***1.36 (0.09,21.52)***	***0.999***
	Comparison	***1,280***	***0.1***		
Officer	Ranch Hand	361	0.3	1.39 (0.09,22.32)	0.999
	Comparison	502	0.2		
Enlisted Flyer	Ranch Hand	160	0.0	--	--
	Comparison	203	0.0		
Enlisted Groundcrew	Ranch Hand	422	0.0	--	--
	Comparison	575	0.0		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks**
All	--	--	
Officer	--	--	
Enlisted Flyer	--	--	
Enlisted Groundcrew	--	--	

--: Estimated relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Table 10-33. (Continued)
Analysis of Hodgkin's Disease

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)**	
Initial Dioxin	**n**	**Percent Yes**	**Estimated Relative Risk (95% C.I.)**	**p-Value**
Low	170	0.0	--	--
Medium	172	0.0		
High	172	0.0		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)			
n	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks**
--	--	--	

--: Statistical analyses not performed due to zero abnormalities.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-33. (Continued)
Analysis of Hodgkin's Disease

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	0.1		
Background RH	372	0.3	2.59 (0.15,43.50)	0.509
Low RH	255	0.0	--	--
High RH	259	0.0	--	--
Low plus High RH	514	0.0	--	--

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Comparison	--			
Background RH	--	--	--	
Low RH	--	--	--	
High RH	--	--	--	
Low plus High RH	--	--	--	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

--: Estimated relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin $\leq$143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.

Table 10-33. (Continued)
Analysis of Hodgkin's Disease

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Yes/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.3 (293)	0.0 (296)	0.0 (297)	0.64 (0.14,2.90)	0.553
5	0.3 (298)	0.0 (292)	0.0 (296)	0.73 (0.27,2.00)	0.563
6[c]	0.3 (297)	0.0 (292)	0.0 (296)	0.78 (0.25,2.44)	0.684

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	867	0.74 (0.11,4.90)	0.746	AGE (p=0.019) DRKYR (p=0.131)
5	867	0.70 (0.13,3.61)	0.661	AGE (p=0.018) DRKYR (p=0.127)
6[d]	866	0.73 (0.12,4.43)	0.725	AGE (p=0.015) DRKYR (p=0.127)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 10-34.
Analysis of Leukemia

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***943***	***0.1***	***1.36 (0.09,21.74)***	***0.999***
	Comparison	***1,280***	***0.1***		
Officer	Ranch Hand	361	0.0	--	--
	Comparison	502	0.0		
Enlisted Flyer	Ranch Hand	160	0.6	--	--
	Comparison	203	0.0		
Enlisted Groundcrew	Ranch Hand	422	0.0	--	--
	Comparison	575	0.2		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks**
All	--	--	
Officer	--	--	
Enlisted Flyer	--	--	
Enlisted Groundcrew	--	--	

--: Estimated relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Table 10-34. (Continued)
Analysis of Leukemia

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	170	0.0	0.61 (0.09,4.14)	0.569
Medium	172	0.6		
High	172	0.0		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
--	--	--	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

--: Adjusted analysis not performed due to the sparse number of abnormalities.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-34. (Continued)
Analysis of Leukemia

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	0.1		
Background RH	372	0.0	--	--
Low RH	255	0.4	4.35 (0.26,70.40)	0.300
High RH	259	0.0	--	--
Low plus High RH	514	0.2	2.10 (0.13,34.67)	0.603

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Comparison	--			
Background RH	--	--	--	
Low RH	--	--	--	
High RH	--	--	--	
Low plus High RH	--	--	--	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

--: Estimated relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$10 ppt.
Low (Ranch Hand): Current Dioxin $>$10 ppt, 10 ppt $<$ Initial Dioxin $\leq$143 ppt.
High (Ranch Hand): Current Dioxin $>$10 ppt, Initial Dioxin $>$143 ppt.

Table 10-34. (Continued)
Analysis of Leukemia

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.0 (293)	0.3 (296)	0.0 (297)	1.10 (0.30,4.06)	0.885
5	0.0 (298)	0.3 (292)	0.0 (296)	1.01 (0.32,3.22)	0.984
6[c]	0.0 (297)	0.3 (292)	0.0 (296)	1.25 (0.36,4.34)	0.728

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
4	--	--	--	
5	--	--	--	
6	--	--	--	

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

--: Adjusted analysis not performed due to the sparse number of abnormalities.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

$p > 0.26$ for all analyses performed). Lifetime alcohol history displayed significant covariate effects in Models 1 and 3. Model 1 also adjusted for age. Low frequencies of the history of non-Hodgkin's lymphoma prevented further statistical analysis.

Results from Models 4, 5, and 6 were nonsignificant for all unadjusted and adjusted analyses (Table 10-35(d,e): $p \geq 0.43$ for each analysis). Because of the sparse number of participants with a history of non-Hodgkin's lymphoma, only the candidate covariates of age, lifetime cigarette smoking history, and lifetime alcohol history were considered. Each final model adjusted for age.

Other Malignant Systemic Neoplasms of Lymphoid and Histiocytic Tissue

Because of the sparse number of participants with a history of other malignant systemic neoplasms of lymphoid and histiocytic tissue, not all unadjusted analyses were possible for Models 1 and 3. All results were nonsignificant (Table 10-36(a-f): $p > 0.47$). Model 2 analyses were not possible. Sample sizes and history percentages are presented in Table 10-36.

Results from Models 4, 5, and 6 were nonsignificant for all analyses (Table 10-36(g,h): $p \geq 0.43$ for each analysis). Because of the sparse number of participants with a history of other malignant systemic neoplasms of lymphoid and histiocytic tissue, only the candidate covariates of age, lifetime cigarette smoking history, and lifetime alcohol history were considered in these models. Each final model adjusted for age.

Multiple Myeloma

Due to the sparse number of participants with a history of multiple myeloma, analyses of Models 1, 2, and 3 were not possible. Sample sizes and frequencies of histories for Models 1, 2, and 3 are presented in Table 10-37(a-f).

Unadjusted analyses of multiple myeloma showed no significant results for Models 4, 5, and 6 (Table 10-37(g,h): $p > 0.78$ for all analyses). Adjusted analyses were not performed due to the sparse number of Ranch Hands with a history of multiple myeloma.

Skin or Systemic Neoplasms

Each Ranch Hand versus Comparison contrast examined with the Model 1 unadjusted analysis of history of a skin or systemic neoplasm was nonsignificant (Table 10-38(a): $p > 0.10$ for each contrast). A marginally significant difference was found in the adjusted overall contrast (Table 10-38(b): $p = 0.096$, Adj. $RR = 1.16$). Adjusted differences were nonsignificant when examined within each occupational category (Table 10-38(b): $p > 0.11$ for remaining contrasts). Age, skin, and eye color displayed significant covariate effects in the final adjusted model.

Each Model 2 analysis revealed a significant negative association between a history of a skin or systemic neoplasm and initial dioxin (Table 10-38(c,d): $p = 0.012$, Est. $RR = 0.84$ for both unadjusted and adjusted). Results indicate that a history of a skin or systemic neoplasm

Table 10-35.
Analysis of Non-Hodgkin's Lymphoma

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***943***	***0.1***	***0.34 (0.04,3.04)***	***0.574***
	Comparison	***1,280***	***0.3***		
Officer	Ranch Hand	361	0.0	--	--
	Comparison	502	0.6		
Enlisted Flyer	Ranch Hand	160	0.0	--	--
	Comparison	203	0.5		
Enlisted Groundcrew	Ranch Hand	422	0.2	--	--
	Comparison	575	0.0		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***0.32 (0.03,2.95)***	***0.267***	AGE (p=0.088) DRKYR (p=0.042)
Officer	--	--	
Enlisted Flyer	--	--	
Enlisted Groundcrew	--	--	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

--: Estimated relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Table 10-35. (Continued)
Analysis of Non-Hodgkin's Lymphoma

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)**	
Initial Dioxin	**n**	**Percent Yes**	**Estimated Relative Risk (95% C.I.)**	**p-Value**
Low	170	0.0	--	--
Medium	172	0.0		
High	172	0.0		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)			
n	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks**
--	--	--	

--: Statistical analyses not performed due to zero abnormalities.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-35. (Continued)
Analysis of Non-Hodgkin's Lymphoma

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	0.2		
Background RH	372	0.3	1.23 (0.11,14.03)	0.865
Low RH	255	0.0	--	--
High RH	259	0.0	--	--
Low plus High RH	514	0.0	--	--

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Comparison	1,044			DRKYR (p=0.013)
Background RH	365	0.84 (0.06,12.57)	0.900	
Low RH	250	--	--	
High RH	252	--	--	
Low plus High RH	512	--	--	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

--: Estimated relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.

Table 10-35. (Continued)
Analysis of Non-Hodgkin's Lymphoma

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Yes/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.3 (293)	0.0 (296)	0.0 (297)	0.57 (0.13,2.61)	0.462
5	0.3 (298)	0.0 (292)	0.0 (296)	0.67 (0.26,1.71)	0.450
6[c]	0.3 (297)	0.0 (292)	0.0 (296)	0.74 (0.25,2.26)	0.624

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	886	0.52 (0.09,3.05)	0.480	AGE (p=0.019)
5	886	0.59 (0.18,1.94)	0.430	AGE (p=0.018)
6[d]	885	0.52 (0.11,2.39)	0.440	AGE (p=0.012)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 10-36.
Analysis of Other Malignant Systemic Neoplasms of Lymphoid and Histiocytic Tissue

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***943***	***0.1***	***1.36 (0.09,21.74)***	***0.999***
	Comparison	***1,280***	***0.1***		
Officer	Ranch Hand	361	0.0	--	--
	Comparison	502	0.2		
Enlisted Flyer	Ranch Hand	160	0.0	--	--
	Comparison	203	0.0		
Enlisted Groundcrew	Ranch Hand	422	0.2	--	--
	Comparison	575	0.0		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks**
All	--	--	
Officer	--	--	
Enlisted Flyer	--	--	
Enlisted Groundcrew	--	--	

--: Estimated relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Table 10-36. (Continued)
Analysis of Other Malignant Systemic Neoplasms of Lymphoid and Histiocytic Tissue

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)**	
Initial Dioxin	**n**	**Percent Yes**	**Estimated Relative Risk (95% C.I.)**	**p-Value**
Low	170	0.0	--	--
Medium	172	0.0		
High	172	0.0		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)			
n	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks**
--	--	--	

--: Statistical analyses not performed due to zero abnormalities.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-36. (Continued)
Analysis of Other Malignant Systemic Neoplasms of Lymphoid and Histiocytic Tissue

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	0.1		
Background RH	372	0.3	2.84 (0.16,50.71)	0.477
Low RH	255	0.0	--	--
High RH	259	0.0	--	--
Low plus High RH	514	0.0	--	--

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Comparison	--			
Background RH	--	--	--	
Low RH	--	--	--	
High RH	--	--	--	
Low plus High RH	--	--	--	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

--: Estimated relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$10 ppt.
Low (Ranch Hand): Current Dioxin $>$10 ppt, 10 ppt $<$ Initial Dioxin $\leq$143 ppt.
High (Ranch Hand): Current Dioxin $>$10 ppt, Initial Dioxin $>$143 ppt.

Table 10-36. (Continued)
Analysis of Other Malignant Systemic Neoplasms of Lymphoid and Histiocytic Tissue

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.3 (293)	0.0 (296)	0.0 (297)	0.57 (0.13,2.61)	0.462
5	0.3 (298)	0.0 (292)	0.0 (296)	0.67 (0.26,1.71)	0.450
6[c]	0.3 (297)	0.0 (292)	0.0 (296)	0.74 (0.25,2.26)	0.624

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	886	0.52 (0.09,3.05)	0.480	AGE (p=0.019)
5	886	0.59 (0.18,1.94)	0.430	AGE (p=0.018)
6[d]	885	0.52 (0.11,2.39)	0.440	AGE (p=0.012)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 10-37.
Analysis of Multiple Myeloma

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***943***	***0.1***	--	--
	Comparison	***1,280***	***0.0***		
Officer	Ranch Hand	361	0.0	--	--
	Comparison	502	0.0		
Enlisted Flyer	Ranch Hand	160	0.0	--	--
	Comparison	203	0.0		
Enlisted Groundcrew	Ranch Hand	422	0.2	--	--
	Comparison	575	0.0		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks**
All	--	--	
Officer	--	--	
Enlisted Flyer	--	--	
Enlisted Groundcrew	--	--	

--: Analyses not performed due to the sparse number of abnormalities.

Table 10-37. (Continued)
Analysis of Multiple Myeloma

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)	p-Value
Low	170	0.6	--	--
Medium	172	0.0		
High	172	0.0		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)			
n	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
--	--	--	

--: Analyses not performed due to the sparse number of abnormalities.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-37. (Continued)
Analysis of Multiple Myeloma

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
Comparison	1,062	0.0		
Background RH	372	0.0	--	--
Low RH	255	0.4	--	--
High RH	259	0.0	--	--
Low plus High RH	514	0.2	--	--

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Comparison	--			
Background RH	--	--	--	
Low RH	--	--	--	
High RH	--	--	--	
Low plus High RH	--	--	--	

--: Analyses not performed due to the sparse number of abnormalities.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$10 ppt.
Low (Ranch Hand): Current Dioxin $>$10 ppt, 10 ppt $<$ Initial Dioxin $\leq$143 ppt.
High (Ranch Hand): Current Dioxin $>$10 ppt, Initial Dioxin $>$143 ppt.

Table 10-37. (Continued)
Analysis of Multiple Myeloma

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.0 (293)	0.3 (296)	0.0 (297)	0.82 (0.20,3.44)	0.781
5	0.0 (298)	0.3 (292)	0.0 (296)	0.89 (0.29,2,75)	0.835
6[c]	0.0 (297)	0.3 (292)	0.0 (296)	0.87 (0.26,2.92)	0.817

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
4	--	--	--	
5	--	--	--	
6	--	--	--	

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

--: Adjusted analyses not performed due to the sparse number of abnormalities.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 10-38.
Analysis of Skin or Systemic Neoplasms

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***933***	***44.9***	***1.16 (0.97,1.37)***	***0.108***
	Comparison	***1,271***	***41.4***		
Officer	Ranch Hand	358	48.0	1.07 (0.82,1.40)	0.679
	Comparison	496	46.4		
Enlisted Flyer	Ranch Hand	158	48.1	1.23 (0.81,1.86)	0.398
	Comparison	202	43.1		
Enlisted Groundcrew	Ranch Hand	417	41.0	1.21 (0.94,1.57)	0.167
	Comparison	573	36.5		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.16 (0.97,1.38)***	***0.096***	AGE ($p<0.001$) SKIN ($p=0.096$) EYE ($p=0.027$)
Officer	1.08 (0.82,1.42)	0.597	
Enlisted Flyer	1.16 (0.76,1.77)	0.497	
Enlisted Groundcrew	1.24 (0.95,1.61)	0.112	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 10-38. (Continued)
Analysis of Skin or Systemic Neoplasms

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	165	48.5	0.84 (0.73,0.97)	0.012
Medium	170	44.7		
High	172	39.0		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
502	0.84 (0.73,0.96)	0.012	EYE (p=0.003) SUN2HR (p=0.033) LAT (p=0.044)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-38. (Continued)
Analysis of Skin or Systemic Neoplasms

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,055	42.0		
Background RH	369	45.0	1.17 (0.92,1.49)	0.208
Low RH	250	48.8	1.29 (0.98,1.70)	0.073
High RH	257	39.3	0.87 (0.66,1.16)	0.348
Low plus High RH	507	44.0	1.06 (0.86,1.32)	0.584

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,055			AGE ($p<0.001$) SKIN ($p=0.017$)
Background RH	368	1.10 (0.87,1.41)	0.426	
Low RH	250	1.25 (0.95,1.66)	0.115	
High RH	257	0.97 (0.73,1.29)	0.837	
Low plus High RH	507	1.10 (0.89,1.37)	0.371	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.

Table 10-38. (Continued)
Analysis of Skin or Systemic Neoplasms

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Yes/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	45.0 (291)	49.0 (290)	39.3 (295)	0.93 (0.85,1.02)	0.141
5	45.6 (296)	44.4 (286)	43.2 (294)	0.96 (0.89,1.04)	0.358
6[c]	45.8 (295)	44.4 (286)	43.2 (294)	0.92 (0.84,1.00)	0.049

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	n	Analysis Results for Log_2 (Current Dioxin + 1) Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	873	0.98 (0.89,1.08)**	0.651**	CURR*EYE (p=0.011) AGE (p<0.001) SUN2HR (p=0.105)
5	873	1.00 (0.92,1.09)**	0.970**	CURR*EYE (p=0.010) AGE (p<0.001) SUN2HR (p=0.092)
6[d]	872	0.96 (0.87,1.04)**	0.313**	CURR*EYE (p=0.019) AGE (p<0.001) SUN2HR (p=0.093)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table F-2-11 for further analysis of this interaction.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

decreased as initial dioxin levels increased. The unadjusted Model 3 analysis revealed that Ranch Hands in the low dioxin category exhibited a marginally significant higher history of a skin or systemic neoplasm than Comparisons (Table 10-38(e): $p=0.073$, Est. RR=1.29). All other Model 3 results were nonsignificant (Table 10-38(e,f): $p>0.11$ for all remaining contrasts). Eye color, reaction of skin to sun after at least 2 hours, and average residential latitude were significant in the Model 2 final adjusted model. Age and skin color were significant in Model 3.

Similar to Model 2, the Model 6 unadjusted analysis revealed a significant inverse association between a history of a skin or systemic neoplasm and current dioxin (Table 10-38(g): $p=0.049$, Est. RR=0.92). History of a skin or systemic neoplasm decreased as current dioxin levels increased. Model 6 adjusted analysis and all analyses from Models 4 and 5 were nonsignificant (Table 10-38(g,h): $p>0.14$ for each analysis). Final models each included age, reaction of skin to sun after at least 2 hours, and the current dioxin-by-eye color interaction. Adjusted results for Models 4, 5, and 6 are based on each final model without the significant interaction. Appendix Table F-2-11 presents relative risk estimates by each eye color grouping.

Laboratory Examination Variables

Prostate-Specific Antigen (Continuous)

Because 2.7 percent (60/2,232) of the prostate-specific antigen measurements were below the test sensitivity limit of 0.2 ng/ml and consequently did not have a true measured value, the continuous analysis was conducted in two parts. First, the proportion of prostate-specific antigen measurements below the sensitivity limit was examined for an association with exposure. Second, only measurements at or above the sensitivity limit detected values were explored for an association with exposure. A natural logarithmic transformation was applied to continuous measurements to enhance normality.

For the first analysis, no associations between the proportion of prostate-specific antigen measurements below the sensitivity limit and group, initial dioxin, or current dioxin were observed (Table 10-39(a-h): $p>0.40$ for each model).

Based on the prostate-specific antigen measurements at or above the test sensitivity limit, Model 1 unadjusted results were nonsignificant, indicating no group association (Table 10-40(a): $p>0.49$ for each contrast). Adjusted analysis revealed a significant group-by-insecticide exposure interaction. Further analysis of this interaction is presented in Appendix Table F-2-12. Comparisons with no insecticide exposure had a significantly larger adjusted mean prostate-specific antigen than Ranch Hands with no insecticide exposure (Appendix Table F-2-12(a): $p=0.012$; Ranch Hand adjusted mean: 0.943 ng/ml, Comparison officer adjusted mean: 1.192 ng/ml). Results were similar when mean differences were examined within the officer stratum (Appendix Table F-2-12(a): $p=0.018$; Ranch Hand officer adjusted mean: 0.934 ng/ml, Comparison officer adjusted mean: 1.192 ng/ml). Other significant covariates in the final adjusted model were lifetime alcohol history, ionizing radiation exposure, and industrial chemical exposure.

Table 10-39.
Analysis of Prostate-Specific Antigen
(Below vs. At or Above Sensitivity Limit)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Below Sensitivity Limit**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***943***	***2.4***	***0.84 (0.50,1.42)***	***0.603***
	Comparison	***1,279***	***2.9***		
Officer	Ranch Hand	361	2.8	0.72 (0.33,1.58)	0.532
	Comparison	502	3.8		
Enlisted Flyer	Ranch Hand	160	2.5	1.70 (0.38,7.71)	0.755
	Comparison	202	1.5		
Enlisted Groundcrew	Ranch Hand	422	2.1	0.81 (0.35,1.88)	0.783
	Comparison	575	2.6		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***0.83 (0.49,1.42)***	***0.498***	AGE (p=0.004)
Officer	0.72 (0.33,1.57)	0.405	ASB (p=0.149)
Enlisted Flyer	1.67 (0.37,7.57)	0.508	IC (p=0.126)
Enlisted Groundcrew	0.82 (0.35,1.89)	0.639	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 10-39. (Continued)
Analysis of Prostate-Specific Antigen
(Below vs. At or Above Sensitivity Limit)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Below Sensitivity Limit**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	170	1.8	0.89 (0.57,1.40)	0.608
Medium	172	3.5		
High	172	2.3		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
	Analysis Results for Log_2 (Initial Dioxin)[c]		
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
514	0.94 (0.60,1.48)	0.794	RACE (p=0.149) IONRAD (p=0.010)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Table 10-39. (Continued)
Analysis of Prostate-Specific Antigen
(Below vs. At or Above Sensitivity Limit)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Below Sensitivity Limit	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	3.0		
Background RH	372	2.7	0.95 (0.46,1.96)	0.882
Low RH	255	2.4	0.76 (0.31,1.83)	0.534
High RH	259	2.7	0.85 (0.37,1.96)	0.700
Low plus High RH	514	2.5	0.80 (0.42,1.55)	0.512

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,062			AGE (p=0.007)
Background RH	372	0.89 (0.43,1.84)	0.749	
Low RH	255	0.71 (0.29,1.73)	0.456	
High RH	259	0.98 (0.42,2.27)	0.957	
Low plus High RH	514	0.83 (0.43,1.61)	0.589	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.

Table 10-39. (Continued)
Analysis of Prostate-Specific Antigen
(Below vs. At or Above Sensitivity Limit)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Below Sensitivity Limit/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	2.4 (293)	2.4 (296)	3.0 (297)	0.97 (0.73,1.29)	0.824
5	2.4 (298)	2.1 (292)	3.4 (296)	1.02 (0.80,1.30)	0.870
6[c]	2.4 (297)	2.1 (292)	3.4 (296)	0.95 (0.73,1.23)	0.677

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	886	0.99 (0.75,1.32)	0.962	RACE (p=0.094) IONRAD (p=0.017)
5	886	1.04 (0.82,1.33)	0.722	RACE (p=0.094) IONRAD (p=0.016)
6[d]	885	0.97 (0.75,1.26)	0.834	RACE (p=0.111) IONRAD (p=0.014)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 10-40.
Analysis of Prostate-Specific Antigen (ng/ml)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***920***	***1.013***	***-0.012 --***	***0.717***
	Comparison	***1,242***	***1.025***		
Officer	Ranch Hand	351	1.131	0.014 --	0.821
	Comparison	483	1.117		
Enlisted Flyer	Ranch Hand	156	1.111	-0.019 --	0.838
	Comparison	199	1.130		
Enlisted Groundcrew	Ranch Hand	413	0.890	-0.028 --	0.492
	Comparison	560	0.918		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	***Ranch Hand***	***900***	****	****	****	GROUP*INS (p=0.004) DRKYR (p=0.114) IONRAD (p=0.004) IC (p=0.023)
	Comparison	***1,223***	****			
Officer	Ranch Hand	348	****	****	****	
	Comparison	476	****			
Enlisted Flyer	Ranch Hand	151	****	****	****	
	Comparison	198	****			
Enlisted Groundcrew	Ranch Hand	401	****	****	****	
	Comparison	549	****			

[a] Transformed from the natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

**** Group-by-covariate interaction ($p \leq 0.01$); adjusted mean, difference of adjusted means, and p-value not presented; refer to Appendix Table F-2-12 for further analysis this interaction.

Note: Analysis based on measurements at or above 0.2 ng/ml (sensitivity limit) only.

Table 10-40. (Continued)
Analysis of Prostate-Specific Antigen (ng/ml)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	167	1.202	1.185	0.052	-0.086 (0.026)	0.001
Medium	166	0.936	0.933			
High	168	0.872	0.888			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	167	1.016**	0.140	-0.036 (0.026)**	0.179**	INIT*AGE (p=0.026) PACKYR (p=0.019) IONRAD (p=0.065) HERB (p=0.122)
Medium	166	0.874**				
High	168	0.898**				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of prostate specific antigen versus log_2 (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table F-2-12 for further analysis of this interaction.

Note: Analysis based on measurements at or above 0.2 ng/ml (sensitivity limit) only.
Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-40. (Continued)
Analysis of Prostate-Specific Antigen (ng/ml)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,030	1.043	1.044		
Background RH	362	1.042	1.032	-0.012 --	0.800
Low RH	249	1.098	1.098	0.054 --	0.342
High RH	252	0.900	0.910	-0.134 --	0.010
Low plus High RH	501	0.998	1.003	-0.040 --	0.287

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[ac]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,014	****			DXCAT*INS (p=0.009)
Background RH	356	****	****	****	AGE (p<0.001) PACKYR (p=0.009) DRKYR (p=0.008)
Low RH	244	****	****	****	
High RH	245	****	****	****	
Low plus High RH	489	****	****	****	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

**** Categorized dioxin-by-covariate interaction ($p \leq 0.01$); adjusted mean, difference of adjusted means, and p-value not presented; refer to Appendix Table F-2-12 for further analysis of this interaction.

Note: Analysis based on measurements at or above 0.2 ng/ml (sensitivity limit) only.
RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.

Table 10-40. (Continued)
Analysis of Prostate-Specific Antigen (ng/ml)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[b]	Current Dioxin Category Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Slope (Std. Error)[c]	p-Value
4	1.045 (286)	1.128 (289)	0.883 (288)	0.009	-0.049 (0.017)	0.005
5	1.058 (291)	1.088 (286)	0.905 (286)	0.009	-0.042 (0.015)	0.005
6[d]	1.053 (290)	1.087 (286)	0.912 (286)	0.010	-0.041 (0.016)	0.010

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[b]	Current Dioxin Category Adjusted Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	0.973 (285)	1.040 (289)	0.911 (288)	0.098	-0.018 (0.017)	0.275	AGE ($p<0.001$) PACKYR ($p=0.001$) INS ($p=0.007$)
5	0.986 (290)	1.005 (286)	0.928 (286)	0.099	-0.019 (0.014)	0.186	AGE ($p<0.001$) PACKYR ($p=0.001$) INS ($p=0.007$)
6[e]	0.975 (289)	1.002 (286)	0.943 (286)	0.101	-0.015 (0.016)	0.353	AGE ($p<0.001$) PACKYR ($p=0.003$) INS ($p=0.006$)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of prostate specific antigen versus log_2 (current dioxin+1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Analysis based on measurements at or above 0.2 ng/ml (sensitivity limit) only.
Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The Model 2 unadjusted analysis revealed a significant inverse association between prostate-specific antigen measurements at or above the test sensitivity limit and initial dioxin (Table 10-40(c): p=0.001, slope=-0.086; low initial dioxin category adjusted mean: 1.185 ng/ml, medium initial dioxin category adjusted mean: 0.933 ng/ml, high initial dioxin category adjusted mean: 0.888 ng/ml). The negative slope indicated prostate-specific antigen measurements among Ranch Hands decreased as initial dioxin measurements increased among Ranch Hands. Results were nonsignificant after covariate adjustment and deletion of the significant interaction between initial dioxin and age (Table 10-40(d): p=0.179). Lifetime cigarette smoking history, ionizing radiation exposure, and herbicide exposure also were significant in the final adjusted model. Analyses stratified by each age category are presented in Appendix Table F-2-12.

The Model 3 unadjusted contrast between Ranch Hands in the high category and Comparisons was significant, with mean prostate-specific antigen in the Comparison group higher than means in the high Ranch Hand group (Table 10-40(e): p=0.010; Comparison mean and high Ranch Hand mean, adjusted for percent body fat at the time of duty in SEA and change in body fat from the time of duty in SEA to the date of the blood draw for dioxin: 1.044 ng/ml and 0.910 ng/ml respectively). Other unadjusted contrasts were nonsignificant (Table 10-40(e): p>0.28 for each remaining contrast). Age, lifetime cigarette smoking history, lifetime alcohol history, and the interaction between categorized dioxin and insecticide exposure displayed significant effects in the final adjusted model. Results stratified by each level of insecticide exposure are presented in Appendix Table F-2-12. Comparisons with no insecticide exposure have a significantly larger adjusted mean prostate-specific antigen than Ranch Hands in the background category with no insecticide exposure (Appendix Table F-2-12(c): p=0.001; Comparison adjusted mean: 1.099 ng/ml, background Ranch Hand category adjusted mean: 0.833 ng/ml). The same pattern between Comparisons and Ranch Hands in the low plus high Ranch Hand category with no insecticide exposure is seen, except that the significance was marginal (p=0.062).

Results of the analysis of prostate-specific antigen measurements at or above the test sensitivity limit from Models 4, 5, and 6 were similar. Each unadjusted association with current dioxin was significant and inverse in direction (Table 10-40(g): p=0.005, Est. Slope=-0.049, p=0.005, Est. Slope=-0.042, p=0.010, Est. Slope=-0.041 for Models 4, 5, and 6). The unadjusted means for the low, medium, and high lipid-adjusted current dioxin categories were 1.045 ng/ml, 1.128 ng/ml, and 0.883 ng/ml respectively. The unadjusted means for the low, medium, and high whole-weight current dioxin categories were 1.058 ng/ml, 1.088 ng/ml, and 0.905 ng/ml respectively. The means, adjusted for total lipids, for the low, medium, and high whole-weight current dioxin categories were 1.053 ng/ml, 1.087 ng/ml, and 0.912 ng/ml respectively. Associations were nonsignificant after covariate adjustment for age, lifetime cigarette smoking history, and insecticide exposure for each model (Table 10-40(h): p>0.18 for each analysis).

Prostate-Specific Antigen (Discrete)

Each contrast from the Model 1 unadjusted analysis of prostate-specific antigen, categorized as normal or abnormal, indicated that differences between Ranch Hands and Comparisons were nonsignificant (Table 10-41(a): p>0.18 for each contrast). The

Table 10-41.
Analysis of Prostate-Specific Antigen
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***943***	***3.6***	***0.73 (0.48,1.13)***	***0.188***
	Comparison	***1,279***	***4.9***		
Officer	Ranch Hand	361	5.0	0.86 (0.47,1.57)	0.724
	Comparison	502	5.8		
Enlisted Flyer	Ranch Hand	160	5.0	0.71 (0.29,1.73)	0.588
	Comparison	202	6.9		
Enlisted Groundcrew	Ranch Hand	422	1.9	0.57 (0.25,1.30)	0.248
	Comparison	575	3.3		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	****	****	GROUP*PACKYR (p=0.009) AGE (p<0.001) RACE (p=0.003) DRKYR (p=0.002) IONRAD (p=0.133) INS (p=0.025)
Officer	****	****	
Enlisted Flyer	****	****	
Enlisted Groundcrew	****	****	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

**** Group-by-covariate interaction ($p \leq 0.01$); adjusted relative risk, confidence interval, and p-value not presented; refer to Appendix Table F-2-13 for further analysis this interaction.

Table 10-41. (Continued)
Analysis of Prostate-Specific Antigen
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	170	6.5	0.61 (0.41,0.90)	0.006
Medium	172	7.0		
High	172	0.6		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
	Analysis Results for Log_2 (Initial Dioxin)[c]		
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
514	0.69 (0.46,1.05)	0.064	AGE ($p<0.001$) PACKYR ($p=0.003$)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 10-41. (Continued)
Analysis of Prostate-Specific Antigen
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	5.0		
Background RH	372	2.4	0.49 (0.24,1.00)	0.050
Low RH	255	5.9	1.14 (0.63,2.06)	0.665
High RH	259	3.5	0.67 (0.33,1.39)	0.282
Low plus High RH	514	4.7	0.91 (0.55,1.49)	0.693

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,044			DXCAT*INS (p=0.030) AGE (p<0.001) RACE (p=0.038) DRKYR (p<0.001) HERB (p=0.027)
Background RH	365	0.31 (0.13,0.69)**	0.005**	
Low RH	250	0.84 (0.42,1.66)**	0.611**	
High RH	252	0.76 (0.34,1.71)**	0.511**	
Low plus High RH	502	0.81 (0.45,1.46)**	0.480**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table F-2-13 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.

Table 10-41. (Continued)
Analysis of Prostate-Specific Antigen
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Abnormal/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	1.7 (293)	6.8 (296)	2.7 (297)	0.99 (0.78,1.25)	0.904
5	2.0 (298)	5.1 (292)	4.1 (296)	1.03 (0.84,1.26)	0.808
6[c]	2.0 (297)	5.1 (292)	4.1 (296)	0.98 (0.79,1.23)	0.886

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	885	1.08 (0.81,1.44)**	0.593**	CURR*DC (p=0.039) AGE (p<0.001) PACKYR (p<0.001)
5	885	1.12 (0.87,1.44)**	0.384**	CURR*DC (p=0.020) AGE (p<0.001) PACKYR (p<0.001)
6[d]	884	1.07 (0.82,1.40)**	0.610**	CURR*DC (p=0.021) AGE (p<0.001) PACKYR (p<0.001)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table F-2-13 for further analysis of this interaction.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

interaction between group and lifetime cigarette smoking history was significant in the adjusted model. Other significant covariates were age, race, lifetime alcohol history, ionizing radiation exposure, and insecticide exposure. Analyses stratified by three lifetime cigarette smoking history categories and three occupational cohorts are presented in Appendix Table F-2-13. Enlisted groundcrew Comparisons with more than 10 pack-years of cigarette smoking had a significantly higher percentage of prostate-specific antigen abnormalities than enlisted groundcrew Ranch Hands with more than 10 pack-years of cigarette smoking (Appendix Table F-2-13(a): $p=0.049$, Adj. $RR=0.32$).

A significant association between prostate-specific antigen and initial dioxin was revealed from the unadjusted analyses of Model 2 (Table 10-41(c): $p=0.006$, Est. $RR=0.61$). The background Ranch Hands versus Comparisons unadjusted contrast from Model 3 also was significant (Table 10-41(e): $p=0.050$, Est. $RR=0.49$). Both relative risk estimates indicate the occurrence of prostate-specific antigen abnormalities decreased as dioxin levels increased. Adjusted results were similar, except the Model 2 result was marginally significant (Table 10-41(d,f): $p=0.064$, Adj. $RR=0.69$ for Model 2 and $p=0.005$, Adj. $RR=0.31$ for Model 3). All other Model 3 contrasts were nonsignificant (Table 10-41(e,f): $p>0.28$ for all remaining contrasts). Model 2 adjusted for age and lifetime cigarette smoking history. Age, race, lifetime alcohol history, herbicide exposure, and a categorized dioxin-by-insecticide exposure interaction were significant in Model 3. Adjusted results were obtained from the final model after deletion of the interaction. Results stratified by each level of insecticide exposure are presented in Appendix Table F-2-13.

Analyses of prostate-specific antigen from Model 4, 5, and 6 were nonsignificant (Table 10-41(g,h): $p>0.38$ for all analyses). Each adjusted result was based upon the final model after deletion of a significant current dioxin-by-degreasing chemical exposure interaction. Appendix Table F-2-13 presents relative risk estimates for each level of degreasing chemical exposure. Each model also adjusted for age and lifetime cigarette smoking history.

Longitudinal Analysis

Longitudinal analyses were conducted on three variables—malignant skin neoplasms, malignant systemic neoplasms, and benign systemic neoplasms—to examine whether changes across time differed with respect to group membership (Model 1), initial dioxin (Model 2), and categorized dioxin (Model 3). The longitudinal analyses for these variables investigated the difference between the 1982 examination and the 1992 examinations. Models 4, 5, and 6 were not examined in longitudinal analyses because current dioxin, the measure of exposure in these models, changes over time and is not available for all participants for 1982 or 1992.

The longitudinal analyses examined relative risks at the 1992 examination for participants classified as normal at the earlier examination. Participants classified as abnormal in 1982 were excluded because the focus of the analyses was on investigating the temporal effects of dioxin during the period between 1982 and 1992. Participants classified as abnormal in 1982 were already abnormal before this period; consequently, only participants classified as normal at the 1982 examination were considered to be at risk when the effects of dioxin over time are explored. The rate of abnormalities under this restriction approximates an incidence rate between 1982 and 1992. All three models were adjusted for

age; Models 2 and 3 also were adjusted for percent body fat at the time of duty in SEA and the change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

Verified Medical Records

Malignant Skin Neoplasms

Among participants who did not have a history of a malignant skin neoplasm in 1982, differences between Ranch Hands and Comparisons were nonsignificant in the Model 1 longitudinal analysis (Table 10-42(a): $p > 0.62$ for all contrasts). All Model 3 contrasts also were nonsignificant (Table 10-42(c): $p > 0.20$ for all contrasts).

For participants with no history of a malignant skin neoplasm in 1982, tests of association between a history of a malignant skin neoplasm and initial dioxin, adjusted for age, revealed a significant inverse relationship in the Model 2 analysis (Table 10-42(b): $p=0.039$, Adj. RR=0.73). The history of a malignant skin neoplasm in 1982, 1985, 1987, and 1992 is consistently lowest among Ranch Hands with the highest initial dioxin levels.

Malignant Systemic Neoplasms

No significant results were seen for each group contrast examined from the Model 1 longitudinal analysis of a history of a malignant systemic neoplasm (Table 10-43(a): $p > 0.12$ for all contrasts).

For Ranch Hands without a history of a malignant systemic neoplasm in 1982, the history of malignant systemic neoplasms in 1992 was inversely related to initial dioxin in the Model 2 longitudinal analysis (Table 10-43(b): $p=0.028$, Adj. RR=0.62). Of the Ranch Hands with no history of a malignant systemic neoplasm in 1982, 6.2 percent with low levels of initial dioxin had a history in 1992, compared to 1.2 percent with high levels of initial dioxin. Model 3 analysis revealed a marginally significant difference between Ranch Hands in the low dioxin category (7.0%) and Comparisons (3.5%) (Table 10-43(c): $p=0.070$, Adj. RR=1.80). All other Model 3 contrasts were nonsignificant ($p > 0.31$ for all remaining contrasts).

Benign Systemic Neoplasms

Longitudinal analysis was performed for participants with no history of a benign systemic neoplasm in 1982. Results from Models 1, 2, and 3 were all nonsignificant, indicating no association between a benign systemic neoplasm and group, initial dioxin, or categorized dioxin (Table 10-44(a-c): $p > 0.14$ for analyses).

DISCUSSION

In ambulatory medicine, the recommendation that asymptomatic individuals undergo periodic physical examinations is based largely on the assumption that such screening may reveal occult malignancy. Although the guidelines for the frequency and content of such

Table 10-42.
Longitudinal Analysis of Malignant Skin Neoplasms

a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Percent Yes/(n) Examination 1982	1985	1987	1992
All	***Ranch Hand***	***5.3 (838)***	***8.3 (817)***	***11.0 (809)***	***14.2 (838)***
	Comparison	***3.5 (994)***	***6.9 (972)***	***8.8 (969)***	***12.5 (994)***
Officer	Ranch Hand	6.0 (331)	10.7 (326)	14.5 (325)	19.6 (331)
	Comparison	3.6 (392)	8.1 (384)	9.7 (380)	16.3 (392)
Enlisted Flyer	Ranch Hand	6.8 (148)	8.9 (146)	11.9 (143)	14.9 (148)
	Comparison	3.7 (161)	6.3 (158)	10.6 (160)	13.0 (161)
Enlisted Groundcrew	Ranch Hand	3.9 (359)	5.8 (345)	7.3 (341)	8.9 (359)
	Comparison	3.4 (441)	6.1 (430)	7.2 (429)	8.8 (441)

Occupational Category	Group	No History in 1982: n in 1992	Percent Yes in 1992	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***794***	***9.5***	***1.04 (0.75,1.43)***	***0.834***
	Comparison	***959***	***9.3***		
Officer	Ranch Hand	311	14.5	1.11 (0.72,1.72)	0.627
	Comparison	378	13.2		
Enlisted Flyer	Ranch Hand	138	8.7	0.91 (0.41,2.01)	0.808
	Comparison	155	9.7		
Enlisted Groundcrew	Ranch Hand	345	5.2	0.93 (0.50,1.76)	0.834
	Comparison	426	5.6		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1992 results; results adjusted for age in 1992.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had no history of malignanat skin neoplasms in 1982 (see Chapter 7, Statistical Methods).

Table 10-42. (Continued)
Longitudinal Analysis of Malignant Skin Neoplasms

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

Initial Dioxin	Percent Yes/(n) Examination			
	1982	1985	1987	1992
Low	6.9 (146)	12.6 (143)	14.5 (145)	17.1 (146)
Medium	5.1 (157)	6.6 (152)	9.2 (153)	13.4 (157)
High	3.8 (159)	5.1 (157)	7.1 (154)	8.8 (159)

Initial Dioxin Category Summary Statistics — No History in 1982			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n in 1992	Percent Yes in 1992	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	136	11.0	0.73 (0.54,1.00)	0.039
Medium	149	8.7		
High	153	5.2		

[a] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of blood draw for dioxin, and age in 1992.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had no history of malignant skin neoplasms in 1982 (see Chapter 7, Statistical Methods).

Table 10-42. (Continued)
Longitudinal Analysis of Malignant Skin Neoplasms

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY

Dioxin Category	Percent Yes/(n) Examination			
	1982	1985	1987	1992
Comparison	3.5 (864)	7.0 (853)	8.6 (854)	12.4 (864)
Background RH	5.2 (325)	8.1 (322)	11.3 (319)	15.4 (325)
Low RH	7.6 (223)	11.9 (218)	13.1 (221)	17.9 (223)
High RH	2.9 (239)	4.3 (234)	7.4 (231)	8.4 (239)
Low plus High RH	5.2 (462)	8.0 (452)	10.2 (452)	13.0 (462)

Dioxin Category	No History in 1982			
	n in 1992	Percent Yes in 1992	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	834	9.2		
Background RH	308	10.7	1.14 (0.74,1.77)	0.551
Low RH	206	11.2	1.17 (0.71,1.92)	0.544
High RH	232	5.6	0.67 (0.36,1.24)	0.202
Low plus High RH	438	8.2	0.92 (0.61,1.40)	0.703

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of blood draw for dioxin, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$10 ppt.
Low (Ranch Hand): Current Dioxin $>$10 ppt, 10 ppt $<$ Initial Dioxin $\leq$143 ppt.
High (Ranch Hand): Current Dioxin $>$10 ppt, Initial Dioxin $>$143 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had no history of malignant skin neoplasms in 1982 (see Chapter 7, Statistical Methods).

Table 10-43.
Longitudinal Analysis of Malignant Systemic Neoplasms

a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Percent Yes/(n) Examination			
		1982	1985	1987	1992
All	***Ranch Hand***	***0.9 (892)***	***1.8 (870)***	***2.4 (861)***	***4.9 (892)***
	Comparison	***1.0 (1,062)***	***1.4 (1,039)***	***1.7 (1,036)***	***4.5 (1,062)***
Officer	Ranch Hand	1.2 (334)	2.4 (329)	3.1 (328)	6.3 (334)
	Comparison	1.2 (403)	2.0 (395)	2.3 (391)	6.7 (403)
Enlisted Flyer	Ranch Hand	1.3 (157)	2.6 (155)	2.6 (152)	7.6 (157)
	Comparison	0.0 (175)	0.0 (172)	1.2 (174)	5.7 (175)
Enlisted Groundcrew	Ranch Hand	0.5 (401)	1.0 (386)	1.8 (381)	2.7 (401)
	Comparison	1.2 (484)	1.3 (472)	1.5 (471)	2.3 (484)

Occupational Category	Group	No History in 1982			
		n in 1992	Percent Yes in 1992	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***884***	***4.1***	***1.24 (0.76,2.00)***	***0.389***
	Comparison	***1051***	***3.5***		
Officer	Ranch Hand	330	5.2	0.96 (0.49,1.88)	0.915
	Comparison	398	5.5		
Enlisted Flyer	Ranch Hand	155	6.5	1.17 (0.46,2.94)	0.741
	Comparison	175	5.7		
Enlisted Groundcrew	Ranch Hand	399	2.3	2.44 (0.79,7.51)	0.121
	Comparison	478	1.1		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1992 results; results adjusted for age in 1992.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had no history of malignant systemic neoplasms in 1982 (see Chapter 7, Statistical Methods).

Table 10-43. (Continued)
Longitudinal Analysis of Malignant Systemic Neoplasms

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

Initial Dioxin	Percent Yes/(n) Examination			
	1982	1985	1987	1992
Low	0.6 (163)	1.9 (160)	3.7 (162)	6.8 (163)
Medium	2.4 (168)	4.3 (162)	4.3 (164)	8.3 (168)
High	0.6 (167)	1.2 (165)	1.2 (161)	1.8 (167)

Initial Dioxin Category Summary Statistics — No History in 1982			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n in 1992	Percent Yes in 1992	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	162	6.2	0.62 (0.39,0.99)	0.028
Medium	164	6.1		
High	166	1.2		

[a] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of blood draw for dioxin, and age in 1992.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had no history of malignant systemic neoplasms in 1982 (see Chapter 7, Statistical Methods).

Table 10-43. (Continued)
Longitudinal Analysis of Malignant Systemic Neoplasms

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY				
	Percent Yes/(n) Examination			
Dioxin Category	1982	1985	1987	1992
Comparison	1.1 (916)	1.3 (905)	1.8 (906)	4.6 (916)
Background RH	0.6 (340)	0.9 (337)	1.5 (334)	4.1 (340)
Low RH	1.2 (245)	2.9 (239)	4.1 (243)	8.2 (245)
High RH	1.2 (253)	2.0 (248)	2.1 (244)	3.2 (253)
Low plus High RH	1.2 (498)	2.5 (487)	3.1 (487)	5.6 (498)

	No History in 1982			
Dioxin Category	n in 1992	Percent Yes in 1992	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	906	3.5		
Background RH	338	3.6	1.01 (0.50,2.03)	0.986
Low RH	242	7.0	1.80 (0.95,3.42)	0.070
High RH	250	2.0	0.73 (0.27,1.96)	0.529
Low plus High RH	492	4.5	1.35 (0.75,2.43)	0.313

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of blood draw for dioxin, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had no history of malignant systemic neoplasms in 1982 (see Chapter 7, Statistical Methods).

Table 10-44.
Longitudinal Analysis of Benign Systemic Neoplasms

a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Percent Yes/(n) Examination 1982	1985	1987	1992
All	***Ranch Hand***	***4.3 (892)***	***7.1 (870)***	***12.4 (861)***	***16.4 (892)***
	Comparison	***5.9 (1,062)***	***8.6 (1,039)***	***12.3 (1,037)***	***15.8 (1,062)***
Officer	Ranch Hand	4.8 (334)	7.0 (329)	12.5 (328)	14.7 (334)
	Comparison	7.7 (403)	10.1 (395)	13.0 (391)	16.4 (403)
Enlisted Flyer	Ranch Hand	5.1 (157)	7.7 (155)	13.8 (152)	19.8 (157)
	Comparison	5.1 (175)	7.6 (172)	14.4 (174)	17.7 (175)
Enlisted Groundcrew	Ranch Hand	3.5 (401)	7.0 (386)	11.8 (381)	16.5 (401)
	Comparison	4.8 (484)	7.6 (472)	10.8 (472)	14.7 (484)

Occupational Category	Group	No History in 1982 n in 1992	Percent Yes in 1992	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***854***	***12.7***	***1.24 (0.93,1.65)***	***0.142***
	Comparison	***999***	***10.5***		
Officer	Ranch Hand	318	10.4	1.12 (0.68,1.84)	0.670
	Comparison	372	9.4		
Enlisted Flyer	Ranch Hand	149	15.4	1.21 (0.64,2.27)	0.556
	Comparison	166	13.3		
Enlisted Groundcrew	Ranch Hand	387	13.4	1.36 (0.89,2.07)	0.152
	Comparison	461	10.4		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1992 results; results adjusted for age in 1992.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had no history of benign systemic neoplasms in 1982 (see Chapter 7, Statistical Methods).

Table 10-44. (Continued)
Longitudinal Analysis of Benign Systemic Neoplasms

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN				
	Percent Yes/(n) Examination			
Initial Dioxin	1982	1985	1987	1992
Low	4.9 (163)	8.1 (160)	14.8 (162)	16.0 (163)
Medium	4.8 (168)	7.4 (162)	9.2 (164)	16.1 (168)
High	4.2 (167)	9.7 (165)	12.4 (161)	16.2 (167)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	No History in 1982			
Initial Dioxin	n in 1992	Percent Yes in 1992	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	155	11.6	1.09 (0.88,1.35)	0.446
Medium	160	11.9		
High	160	12.5		

[a] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of blood draw for dioxin, and age in 1992.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had no history of benign systemic neoplasms in 1982 (see Chapter 7, Statistical Methods).

Table 10-44. (Continued)
Longitudinal Analysis of Benign Systemic Neoplasms

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY				
	Percent Yes/(n) Examination			
Dioxin Category	1982	1985	1987	1992
Comparison	6.1 (916)	9.0 (905)	12.5 (907)	15.7 (916)
Background RH	4.1 (340)	5.6 (337)	12.9 (334)	16.8 (340)
Low RH	5.7 (245)	9.2 (239)	14.0 (243)	16.3 (245)
High RH	3.6 (253)	7.7 (248)	10.3 (244)	15.8 (253)
Low plus High RH	4.6 (498)	8.4 (487)	12.1 (487)	16.1 (498)

	No History in 1982			
Dioxin Category	n in 1992	Percent Yes in 1992	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	860	10.2		
Background RH	326	13.2	1.29 (0.87,1.92)	0.199
Low RH	231	11.3	1.09 (0.68,1.73)	0.729
High RH	244	12.7	1.39 (0.89,2.17)	0.148
Low plus High RH	475	12.0	1.23 (0.86,1.76)	0.254

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of blood draw for dioxin, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had no history of benign systemic neoplasms in 1982 (see Chapter 7, Statistical Methods).

examinations are subject to debate, there is no doubt that early detection affords the best and, in most forms of cancer, the only chance for cure. While no one screening test is absolutely reliable, the scope and depth of the protocol employed in this longitudinal study far exceed that considered routine in clinical practice.

As the anatomic point of contact with industrial toxins and as the only organ system with a clearly defined clinical endpoint (i.e., chloracne) for TCDD exposure, the skin deserves the special emphasis it has received in this study. Although there is no evidence that TCDD exposure causes—or that chloracne is associated with—basal cell carcinomas, the Ranch Hand cohort was found to be at increased risk for the occurrence of these skin cancers in each of the three prior examination cycles. As in previous examination cycles, skin lesions considered to be suggestive of skin cancer were biopsied. Though blind to the participants' exposure status, examiners performed a similar number of biopsies in the Ranch Hand (20 out of 952) and Comparison (34 out of 1,281) cohorts.

In the current analyses, Ranch Hands continue to have a slightly higher prevalence of benign and malignant skin neoplasms than Comparisons, including that of basal cell skin cancers at all sites (11.3% of Ranch Hands vs. 10.2% of Comparisons). However, these group differences are no longer significant. Furthermore, consistent with results reported in the Serum Dioxin Analysis Report of the 1987 examinations, in many analyses employing current serum dioxin, a statistically significant inverse dose-response was documented with the prevalence of basal cell skin cancer decreasing as the level of serum dioxin increased. Similar associations were noted as well in the analyses of squamous cell carcinomas and melanoma, though the results were not statistically significant.

In the 1987 examinations, one of the few statistically significant findings was an increased history of a benign systemic neoplasm in the Ranch Hand cohort in a pattern consistent with a dose-response effect. At that time, Ranch Hands with the highest levels of current serum dioxin had a significantly higher incidence of benign systemic neoplasms (such as lipomas) than Comparisons (10.2% vs. 4.1%). In the current analyses, the prevalence was similar in Ranch Hands and Comparisons (16.4% vs. 15.6%) and there was no evidence suggesting a dose-response effect in any of the analyses.

Consistent with all previous examinations, none of the analyses revealed any significant group differences in the prevalence of systemic malignancies in the Ranch Hand and Comparison cohorts. Furthermore, in Ranch Hands, there was no evidence for an increased risk of any systemic malignancy in association with either the current or extrapolated initial levels of serum dioxin.

The mortality associated with certain neoplasms is of particular interest in this longitudinal study. Four Comparisons and no Ranch Hands with soft tissue sarcoma have died, and eight Comparisons and one Ranch Hand with non-Hodgkin's lymphoma are deceased. With the 19,111 Comparisons and 1,261 Ranch Hands under study for mortality, the history of the malignancies do indicate a detriment to Ranch Hands.

The 1992 examinations were the first to incorporate the PSA in the examination. This test has proven highly valuable in the early detection of silent prostate cancer. Though group

differences were not statistically significant, Comparisons had a slightly higher mean PSA than Ranch Hands (1.025 ng/ml vs. 1.013 ng/ml) and were more likely to have an abnormally elevated PSA by discrete analysis (4.9% vs. 3.6%).

The protocol of the current examinations included close surveillance of the 37 Ranch Hands and 70 Comparisons who had PSA levels equal to or greater than 4.0 ng/ml. With more than 90 percent followup to date, biopsy-proven cancer of the prostate has been diagnosed in 9 Ranch Hands and 8 Comparisons.

Dependent variable-covariate associations confirm an increased risk of various cancers in association with well-established risk factors including age, cigarette use, and alcohol consumption. The finding of a higher prevalence of elevated PSA levels in Black participants is of interest and may reflect a race-specific variation not yet recognized.

In summary, at the end of a decade of surveillance, Ranch Hands and Comparisons appear to be at equal risk for the development of all forms of neoplastic disease. Longitudinal analyses have found no significant group differences in the incidence of benign or malignant neoplasms including those that are thought by some to be related to herbicide exposure (i.e., Hodgkin's disease, non-Hodgkin's lymphoma, and STS).

SUMMARY

A number of verified neoplastic conditions, including specific skin and systemic neoplasia endpoints, were examined in the neoplasia assessment, as well as one laboratory test (prostate-specific antigen). Each health endpoint was tested for any statistically significant relationship with group (Model 1), initial dioxin (Model 2), categorized dioxin (Model 3), current lipid-adjusted dioxin (Model 4), current whole-weight dioxin (Model 5), and current whole-weight dioxin adjusted for total lipids (Model 6). Results are summarized and presented in Tables 10-45 through 10-48. A summary of group-by-covariate and dioxin-by-covariate interactions is found in Table 10-49.

Model 1: Group Analysis

The Model 1 analysis of all the neoplasia endpoints detected only a marginally significant difference between Ranch Hands and Comparisons for one endpoint (skin neoplasms). All other Model 1 analyses were nonsignificant or were not performed due to the sparse number of cases. The ability to detect significant differences for most of the site-specific systemic neoplasms was limited by the small number of participants with a history of a neoplasm at any given site. Prostate-specific antigen exhibited highly significant interactions with insecticide exposure and lifetime cigarette smoking history in the continuous and discrete forms respectively. Unadjusted results for both forms of prostate-specific antigen were nonsignificant.

Model 2: Initial Dioxin Analysis

In contrast to Model 1, several significant and marginally significant associations were found from the Model 2 analyses. Each significant association was from an inverse

Table 10-45.
Summary of Group Analyses (Model 1) for Neoplasia Variables
(Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Verified Medical Records				
Skin Neoplasms (D)	NS*	NS	NS	NS
Malignant Skin Neoplasms (D)	NS	NS	NS	ns
Benign Skin Neoplasms (D)	NS	NS	NS	NS
Skin Neoplasms of Uncertain Behavior or Unspecified Nature (D)	ns	ns	--	ns
Basal Cell Carcinomas (All Sites Combined) (D)	NS	NS	NS	ns
Basal Cell Carcinomas (Ear, Face, Head, and Neck) (D)	NS	NS	NS	NS
Basal Cell Carcinomas (Trunk) (D)	NS	NS	NS	ns
Basal Cell Carcinomas (Upper Extremities) (D)	NS	NS	NS	ns
Basal Cell Carcinomas (Lower Extremities) (D)	ns	NS	--	--
Squamous Cell Carcinomas (D)	NS	ns	NS	NS
Nonmelanomas (D)	NS	NS	NS	ns
Melanomas (D)	NS	NS	--	NS
Systemic Neoplasms (D)	NS	ns	NS	NS
Malignant Systemic Neoplasms (D)	NS	ns	NS	NS
Benign Systemic Neoplasms (D)	NS	ns	NS	NS
Systemic Neoplasms of Uncertain Behavior or Unspecified Nature (D)	ns	NS	--	ns
Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck) (D)	NS	NS	ns	NS
Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx) (D)	ns	ns	NS	ns
Malignant Systemic Neoplasms (Esophagus) (D)	--	--	--	--
Malignant Systemic Neoplasms (Brain) (D)	NS	--	--	--
Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum) (D)	--	--	--	--
Malignant Systemic Neoplasms (Thyroid Gland) (D)	NS	NS	--	--
Malignant Systemic Neoplasms (Bronchus and Lung) (D)	NS	NS	ns	NS

Table 10-45. (Continued)
Summary of Group Analyses (Model 1) for Neoplasia Variables
(Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Malignant Systemic Neoplasms (Colon and Rectum) (D)	NS	NS	--	--
Malignant Systemic Neoplasms (Kidney and Bladder) (D)	NS	ns	--	--
Malignant Systemic Neoplasms (Prostate) (D)	ns	ns	NS	NS
Malignant Systemic Neoplasms (Testicles) (D)	--	--	--	--
Malignant Systemic Neoplasms (Ill-Defined Sites) (D)	ns	--	--	--
Malignant Systemic Neoplasms (Connective and Other Soft Tissue) (D)	--	--	--	--
Carcinomas in Situ of the Penis, Other, and Unspecified Sites (D)	NS	--	--	--
Hodgkin's Disease (D)	NS	NS	--	--
Leukemia (D)	NS	--	--	--
Non-Hodgkin's Lymphoma (D)	ns	--	--	--
Other Malignant Systemic Neoplasms of Lymphoid and Histiocytic Tissue (D)	NS	--	--	--
Multiple Myeloma (D)	--	--	--	--
Skin or Systemic Neoplasms (D)	NS	NS	NS	NS
Laboratory				
Prostate-Specific Antigen (D: Below vs. At or Above Sensitivity Limit)	NS	NS	ns	NS
Prostate-Specific Antigen (C: Measurements At or Above Sensitivity Limit)	ns	NS	ns	ns
Prostate-Specific Antigen (D)	ns	ns	ns	ns

C: Continuous analysis.
D: Discrete analysis.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant ($p > 0.10$).
NS*: Marginally significant ($0.05 < p \leq 0.10$).
Note: A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 10-45. (Continued)
Summary of Group Analyses (Model 1) for Neoplasia Variables
(Ranch Hands vs. Comparisons)

Variable	ADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Verified Medical Records				
Skin Neoplasms (D)	NS*	NS	NS	NS
Malignant Skin Neoplasms (D)	NS	NS	NS	ns
Benign Skin Neoplasms (D)	NS	NS	NS	NS
Skin Neoplasms of Uncertain Behavior or Unspecified Nature (D)	ns	ns	--	ns
Basal Cell Carcinomas (All Sites Combined) (D)	NS	NS	NS	ns
Basal Cell Carcinomas (Ear, Face, Head, and Neck) (D)	NS	NS	NS	NS
Basal Cell Carcinomas (Trunk) (D)	ns	ns	NS	ns
Basal Cell Carcinomas (Upper Extremities) (D)	NS	NS	NS	ns
Basal Cell Carcinomas (Lower Extremities) (D)	--	--	--	--
Squamous Cell Carcinomas (D)	NS	NS	NS	NS
Nonmelanomas (D)	NS	NS	NS	NS
Melanomas (D)	NS	NS	--	NS
Systemic Neoplasms (D)	NS	ns	NS	NS
Malignant Systemic Neoplasms (D)	NS	ns	NS	NS
Benign Systemic Neoplasms (D)	NS	ns	NS	NS
Systemic Neoplasms of Uncertain Behavior or Unspecified Nature (D)	ns	NS	--	ns
Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck) (D)	NS	NS	ns	NS
Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx) (D)	NS	ns	NS	ns
Malignant Systemic Neoplasms (Esophagus) (D)	--	--	--	--
Malignant Systemic Neoplasms (Brain) (D)	--	--	--	--
Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum) (D)	--	--	--	--
Malignant Systemic Neoplasms (Thyroid Gland) (D)	NS	NS	--	--
Malignant Systemic Neoplasms (Bronchus and Lung) (D)	NS	NS	ns	NS

Table 10-45. (Continued)
Summary of Group Analyses (Model 1) for Neoplasia Variables
(Ranch Hands vs. Comparisons)

Variable	ADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Malignant Systemic Neoplasms (Colon and Rectum) (D)	NS	NS	--	--
Malignant Systemic Neoplasms (Kidney and Bladder) (D)	NS	ns	--	--
Malignant Systemic Neoplasms (Prostate) (D)	ns	ns	NS	NS
Malignant Systemic Neoplasms (Testicles) (D)	--	--	--	--
Malignant Systemic Neoplasms (Ill-Defined Sites) (D)	ns	--	--	--
Malignant Systemic Neoplasms (Connective and Other Soft Tissue) (D)	--	--	--	--
Carcinomas of the Penis, Other, and Unspecified Sites (D)	--	--	--	--
Hodgkin's Disease (D)	--	--	--	--
Leukemia (D)	--	--	--	--
Non-Hodgkin's Lymphoma (D)	ns	--	--	--
Other Malignant Systemic Neoplasms of Lymphoid and Histiocytic Tissue (D)	--	--	--	--
Multiple Myeloma (D)	--	--	--	--
Skin or Systemic Neoplasms (D)	NS	NS	NS	NS
Laboratory				
Prostate-Specific Antigen (D: Below vs. At or Above Sensitivity Limit)	ns	ns	NS	ns
Prostate-Specific Antigen (C: Measurements At or Above Sensitivity Limit)	****	****	****	****
Prostate-Specific Antigen (D)	****	****	****	****

C: Continuous analysis.
D: Discrete analysis.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant ($p > 0.10$).
NS*: Marginally significant ($0.05 < p \leq 0.10$).
**** Group-by-covariate interaction ($p \leq 0.01$); refer to Appendix F-2 for further analysis of this interaction.
Note: A capital "NS" denotes a relative risk 1.00 or greater; a lower case "ns" denotes relative risk less than 1.00.

Table 10-46.
Summary of Initial Dioxin Analyses (Model 2) for Neoplasia Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Verified Medical Records		
Skin Neoplasms (D)	-<0.001	-<0.001
Malignant Skin Neoplasms (D)	-0.006	****
Benign Skin Neoplasms (D)	ns*	ns*
Skin Neoplasms of Uncertain Behavior or Unspecified Nature (D)	ns	--
Basal Cell Carcinomas (All Sites Combined) (D)	-0.013	-0.023
Basal Cell Carcinomas (Ear, Face, Head, and Neck) (D)	-0.017	-0.006
Basal Cell Carcinomas (Trunk) (D)	ns	ns
Basal Cell Carcinomas (Upper Extremities) (D)	ns*	ns*
Basal Cell Carcinomas (Lower Extremities) (D)	--	--
Squamous Cell Carcinomas (D)	ns	ns
Nonmelanomas (D)	-0.007	**(-0.032)
Melanomas (D)	ns	-0.021
Systemic Neoplasms (D)	ns	NS
Malignant Systemic Neoplasms (D)	-0.004	****
Benign Systemic Neoplasms (D)	NS	NS
Systemic Neoplasms of Uncertain Behavior or Unspecified Nature (D)	ns	ns
Malignant Systemic Neoplasms (Eye, Ear, Face, Head, or Neck) (D)	ns	****
Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx) (D)	NS	NS
Malignant Systemic Neoplasms (Esophagus) (D)	--	--
Malignant Systemic Neoplasms (Brain) (D)	--	--
Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum) (D)	--	--
Malignant Systemic Neoplasms (Thyroid Gland) (D)	-0.044	-0.044
Malignant Systemic Neoplasms (Bronchus and Lung) (D)	ns	ns
Malignant Systemic Neoplasms (Colon and Rectum) (D)	ns	ns

Table 10-46. (Continued)
Summary of Initial Dioxin Analyses (Model 2) for Neoplasia Variables
(Ranch Hands Only)

Variable	Unadjusted	Adjusted
Malignant Systemic Neoplasms (Kidney and Bladder) (D)	ns	ns
Malignant Systemic Neoplasms (Prostate) (D)	ns	ns
Malignant Systemic Neoplasms (Testicles) (D)	ns	ns
Malignant Systemic Neoplasms (Ill-Defined Sites) (D)	--	--
Malignant Systemic Neoplasms (Connective and Other Soft Tissues) (D)	--	--
Carcinomas in Situ of the Penis, Other, and Unspecified Sites (D)	ns	--
Hodgkin's Disease (D)	--	--
Leukemia (D)	ns	--
Non-Hodgkin's Lymphoma (D)	--	--
Other Malignant Neoplasms of Lymphoid and Histiocytic Tissue (D)	--	--
Multiple Myeloma (D)	--	--
Skin or Systemic Neoplasms (D)	-0.012	-0.012
Laboratory		
Prostate-Specific Antigen (D: Below vs. At or Above Sensitivity Limit)	ns	ns
Prostate-Specific Antigen (C: Measurements At or Above Sensitivity Limit)	-0.001	**(ns)
Prostate-Specific Antigen (D)	-0.006	ns*

C: Continuous analysis.
D: Discrete analysis.
-: Relative risk <1.00 for discrete analysis or slope negative for continuous analysis.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant ($p>0.10$).
ns*: Marginally significant ($0.05<p\leq0.10$).
**(ns): Log_2 (initial dioxin)-by-covariate interaction ($0.01<p\leq0.05$); not significant when interaction is deleted; refer to Appendix F-2 for further analysis of this interaction.
**(0.032): Log_2 (initial dioxin)-by-covariate interaction ($0.01<p\leq0.05$); significant ($p=0.032$) when interaction is deleted; refer to Appendix F-2 for further analysis of this interaction.
**** Log_2 (initial dioxin)-by-covariate interaction ($p\leq0.01$); refer to Appendix F-2 for further analysis of this interaction.
Note: P-value given if $p\leq0.05$.
A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

Table 10-47.
Summary of Categorized Dioxin Analyses (Model 3) for Neoplasia Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Verified Medical Records				
Skin Neoplasms (D)	+0.043	+0.019	ns*	NS
Malignant Skin Neoplasms (D)	NS	+0.036	ns*	NS
Benign Skin Neoplasms (D)	NS*	NS	ns	NS
Skin Neoplasms of Uncertain Behavior or Unspecified Nature (D)	NS	ns	ns	ns
Basal Cell Carcinomas (All Sites Combined) (D)	NS	NS*	ns*	NS
Basal Cell Carcinomas (Ear, Face, Head, and Neck) (D)	NS*	+0.042	ns*	NS
Basal Cell Carcinomas (Trunk) (D)	NS	NS	ns	NS
Basal Cell Carcinomas (Upper Extremities) (D)	NS	ns	ns	ns
Basal Cell Carcinomas (Lower Extremities) (D)	NS	--	--	--
Squamous Cell Carcinomas (D)	NS	NS	ns	NS
Nonmelanomas (D)	NS	+0.042	ns*	NS
Melanomas (D)	NS	NS*	NS	NS
Systemic Neoplasms (D)	ns	NS	ns	NS
Malignant Systemic Neoplasms (D)	NS	+0.024	ns	NS
Benign Systemic Neoplasms (D)	NS	NS	NS	NS
Systemic Neoplasms of Uncertain Behavior or Unspecified Nature (D)	ns	NS	ns	ns
Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck) (D)	NS	NS	NS	NS
Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx) (D)	ns	ns	NS	NS
Malignant Systemic Neoplasms (Esophagus) (D)	--	--	--	--
Malignant Systemic Neoplasms (Brain) (D)	--	--	--	--

Table 10-47. (Continued)
Summary of Categorized Dioxin Analyses (Model 3) for Neoplasia Variables
(Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum) (D)	--	--	--	--
Malignant Systemic Neoplasms (Thyroid Gland) (D)	--	--	--	--
Malignant Systemic Neoplasms (Bronchus and Lung) (D)	NS	NS	--	NS
Malignant Systemic Neoplasms (Colon and Rectum) (D)	NS	+0.034	--	NS
Malignant Systemic Neoplasms (Kidney and Bladder) (D)	NS	NS	NS	NS
Malignant Systemic Neoplasms (Prostate) (D)	ns	NS	ns	ns
Malignant Systemic Neoplasms (Testicles) (D)	--	--	--	--
Malignant Systemic Neoplasms (Ill-Defined Sites) (D)	--	--	--	--
Malignant Systemic Neoplasms (Connective and Other Soft Tissues) (D)	--	--	--	--
Carcinomas in Situ of the Penis, Other, and Unspecified Sites (D)	--	NS	--	NS
Hodgkin's Disease (D)	NS	--	--	--
Leukemia (D)	--	NS	--	NS
Non-Hodgkin's Lymphoma (D)	NS	--	--	--
Other Malignant Neoplasms of Lymphoid and Histiocytic Tissue (D)	NS	--	--	--
Multiple Myeloma (D)	--	--	--	--
Skin or Systemic Neoplasms (D)	NS	NS*	ns	NS

Table 10-47. (Continued)
Summary of Categorized Dioxin Analyses (Model 3) for Neoplasia Variables
(Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Laboratory				
Prostate-Specific Antigen (D: Below vs. At or Above Sensitivity Limit)	ns	ns	ns	ns
Prostate-Specific Antigen (C: Measurements At or Above Sensitivity Limit)	ns	NS	-0.010	ns
Prostate-Specific Antigen (D)	-0.050	NS	ns	ns

C: Continuous analysis.
D: Discrete analysis.
+: Relative risk $\geq$ 1.00.
-: Relative risk $<$ 1.00 for discrete analysis or difference of means negative for continuous analysis.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant ($p > 0.10$).
NS* or ns*: Marginally significant ($0.05 < p \leq 0.10$).
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 10-47. (Continued)
Summary of Categorized Dioxin Analyses (Model 3) for Neoplasia Variables
(Ranch Hands vs. Comparisons)

Variable	ADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Verified Medical Records				
Skin Neoplasms (D)	NS*	+0.021	ns	NS
Malignant Skin Neoplasms (D)	**(NS)	**(NS*)	**(ns)	**(NS)
Benign Skin Neoplasms (D)	NS*	NS	ns	NS
Skin Neoplasms of Uncertain Behavior or Unspecified Nature (D)	NS	ns	ns	ns
Basal Cell Carcinomas (All Sites Combined) (D)	NS	NS	ns	NS
Basal Cell Carcinomas (Ear, Face, Head, and Neck) (D)	NS	NS*	ns	NS
Basal Cell Carcinomas (Trunk) (D)	**(ns)	**(NS)	**(ns)	**(ns)
Basal Cell Carcinomas (Upper Extremities) (D)	NS	ns	ns	ns
Basal Cell Carcinomas (Lower Extremities) (D)	--	--	--	--
Squamous Cell Carcinomas (D)	NS	NS	NS	NS
Nonmelanomas (D)	NS	NS*	ns	NS
Melanomas (D)	ns	NS	ns	NS
Systemic Neoplasms (D)	ns	NS	NS	NS
Malignant Systemic Neoplasms (D)	ns	NS*	ns	NS
Benign Systemic Neoplasms (D)	ns	NS	NS	NS
Systemic Neoplasms of Uncertain Behavior or Unspecified Nature (D)	ns	NS	ns	ns
Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck) (D)	**(NS)	**(NS)	**(NS)	**(NS)
Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx) (D)	ns	ns	NS	NS
Malignant Systemic Neoplasms (Esophagus) (D)	--	--	--	--

Table 10-47. (Continued)
Summary of Categorized Dioxin Analyses (Model 3) for Neoplasia Variables (Ranch Hands vs. Comparisons)

Variable	ADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Malignant Systemic Neoplasms (Brain) (D)	--	--	--	--
Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum) (D)	--	--	--	--
Malignant Systemic Neoplasms (Thyroid Gland) (D)	--	--	--	--
Malignant Systemic Neoplasms (Bronchus and Lung) (D)	NS	NS	--	NS
Malignant Systemic Neoplasms (Colon and Rectum) (D)	NS	+0.034	--	NS
Malignant Systemic Neoplasms (Kidney and Bladder)	NS	NS	NS	NS
Malignant Systemic Neoplasms (Prostate)	****	****	****	****
Malignant Systemic Neoplasms (Testicles)	--	--	--	--
Malignant Systemic Neoplasms (Ill-Defined Sites)	--	--	--	--
Malignant Systemic Neoplasms (Connective and Other Soft Tissues)	--	--	--	--
Carcinomas in Situ of the Penis, Other, and Unspecified Sites	--	--	--	--
Hodgkin's Disease	--	--	--	--
Leukemia	--	--	--	--
Non-Hodgkin's Lymphoma	ns	--	--	--
Other Malignant Neoplasms of Lymphoid and Histiocytic Tissue	--	--	--	--
Multiple Myeloma	--	--	--	--
Skin or Systemic Neoplasms	NS	NS	ns	NS

Table 10-47. (Continued)
Summary of Categorized Dioxin Analyses (Model 3) for Neoplasia Variables (Ranch Hands vs. Comparisons)

Variable	ADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Laboratory				
Prostate-Specific Antigen (D: Below vs. At or Above Sensitivity Limit)	ns	ns	ns	ns
Prostate-Specific Antigen (C: Measurements At or Above Sensitivity Limit)	****	****	****	****
Prostate-Specific Antigen (D)	**(-0.005)	**(ns)	**(ns)	**(ns)

C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00.
-: Relative risk < 1.00.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant ($p > 0.10$).
NS*: Marginally significant ($0.05 < p \leq 0.10$).
**(NS) or **(ns): Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); not significant when interaction is deleted; refer to Appendix F-2 for further analysis of this interaction.
**(-0.005): Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); significant ($p = 0.005$) when interaction is deleted; refer to Appendix F-2 for further analysis of this interaction.
**** Categorized dioxin-by-covariate interaction ($p \leq 0.01$); refer to Appendix F-2 for further analysis of this interaction.
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes a relative risk 1.00 or greater; a lower case "ns" denotes relative risk less than 1.00.

Table 10-48.
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Neoplasia Variables (Ranch Hands Only)

Variable	UNADJUSTED		
	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
Verified Medical Records			
Skin Neoplasms (D)	-0.011	ns*	-0.002
Malignant Skin Neoplasms (D)	-0.038	ns	-0.021
Benign Skin Neoplasms (D)	ns*	ns	-0.029
Skin Neoplasms of Uncertain Behavior or Unspecified Nature (D)	ns	ns	ns
Basal Cell Carcinomas (All Sites Combined) (D)	ns*	ns	-0.032
Basal Cell Carcinomas (Ear, Face, Head, and Neck) (D)	-0.016	ns*	-0.009
Basal Cell Carcinomas (Trunk) (D)	ns	ns	ns
Basal Cell Carcinomas (Upper Extremities) (D)	ns	ns	ns
Basal Cell Carcinomas (Lower Extremities) (D)	ns	NS	ns
Squamous Cell Carcinomas (D)	ns	ns	ns
Nonmelanomas (D)	-0.034	ns	-0.016
Melanomas (D)	ns	ns	NS
Systemic Neoplasms (D)	NS	NS	NS
Malignant Systemic Neoplasms (D)	ns	ns	ns
Benign Systemic Neoplasms (D)	NS	NS	NS
Systemic Neoplasms of Uncertain Behavior or Unspecified Nature (D)	ns	ns	ns
Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck) (D)	ns	ns	NS
Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx) (D)	NS	NS	NS
Malignant Systemic Neoplasms (Esophagus) (D)	--	--	--
Malignant Systemic Neoplasms (Brain) (D)	ns	ns	--
Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum) (D)	ns	ns	ns
Malignant Systemic Neoplasms (Thyroid Gland) (D)	ns	ns	ns

Table 10-48. (Continued)
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Neoplasia Variables (Ranch Hands Only)

Variable	UNADJUSTED		
	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
Malignant Systemic Neoplasms (Bronchus and Lung) (D)	ns	ns	ns
Malignant Systemic Neoplasms (Colon and Rectum) (D)	NS	NS	ns
Malignant Systemic Neoplasms (Kidney and Bladder) (D)	ns	NS	ns
Malignant Systemic Neoplasms (Prostate) (D)	ns	ns	ns
Malignant Systemic Neoplasms (Testicles) (D)	NS	NS	NS
Malignant Systemic Neoplasms (Ill-Defined Sites) (D)	--	--	--
Malignant Systemic Neoplasms (Connective and Other Soft Tissue) (D)	--	--	--
Carcinomas in Situ (Penis, Other, and Unspecified Sites) (D)	ns	ns	ns
Hodgkin's Disease (D)	ns	ns	ns
Leukemia (D)	NS	NS	NS
Non-Hodgkin's Lymphoma (D)	ns	ns	ns
Other Malignant Neoplasms of Lymphoid and Histiocytic Tissue (D)	ns	ns	ns
Multiple Myeloma (D)	ns	ns	ns
Skin or Systemic Neoplasms (D)	ns	ns	-0.049
Laboratory			
Prostate-Specific Antigen (D: Below vs. At or Above Sensitivity Limit)	ns	NS	ns
Prostate-Specific Antigen (C: Measurements At or Above Sensitivity Limit)	-0.005	-0.005	-0.010
Prostate-Specific Antigen (D)	ns	NS	ns

C: Continuous analysis.
D: Discrete analysis.
-: Relative risk < 1.00 for discrete analysis or slope negative for continuous analysis.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant ($p > 0.10$).
ns*: Marginally significant ($0.05 < p \leq 0.10$).
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes a relative risk 1.00 or greater; a lower case "ns" denotes relative risk less than 1.00.

Table 10-48. (Continued)
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Neoplasia Variables (Ranch Hands Only)

Variable	ADJUSTED		
	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
Verified Medical Records			
Skin Neoplasms (D)	ns*	**(ns)	**(-0.008)
Malignant Skin Neoplasms (D)	ns	ns	ns
Benign Skin Neoplasms (D)	-0.034	**(ns*)	**(-0.012)
Skin Neoplasms of Uncertain Behavior or Unspecified Nature (D)	--	--	--
Basal Cell Carcinomas (All Sites Combined) (D)	ns	ns	**(ns)
Basal Cell Carcinomas (Ear, Face, Head, and Neck) (D)	ns	ns	ns*
Basal Cell Carcinomas (Trunk) (D)	**(NS)	**(NS)	**(NS)
Basal Cell Carcinomas (Upper Extremities) (D)	ns	ns	ns
Basal Cell Carcinomas (Lower Extremities) (D)	--	--	--
Squamous Cell Carcinomas (D)	ns	NS	NS
Nonmelanomas (D)	ns	ns	ns
Melanomas (D)	NS	NS	NS
Systemic Neoplasms (D)	NS	NS	NS
Malignant Systemic Neoplasms (D)	**(NS)	**(NS)	**(NS)
Benign Systemic Neoplasms (D)	NS	NS	NS
Systemic Neoplasms of Uncertain Behavior or Unspecified Nature (D)	**(ns)	**(ns)	**(ns)
Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck) (D)	NS	NS	NS
Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx) (D)	NS*	NS*	NS*
Malignant Systemic Neoplasms (Esophagus) (D)	--	--	--
Malignant Systemic Neoplasms (Brain) (D)	--	--	--
Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum) (D)	ns	ns	ns
Malignant Systemic Neoplasms (Thyroid Gland) (D)	ns	ns	ns
Malignant Systemic Neoplasms (Bronchus and Lung) (D)	ns	NS	ns
Malignant Systemic Neoplasms (Colon and Rectum) (D)	NS	NS	NS
Malignant Systemic Neoplasms (Kidney and Bladder) (D)	NS	NS	ns
Malignant Systemic Neoplasms (Prostate) (D)	**(NS)	**(NS)	**(NS)

Table 10-48. (Continued)
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Neoplasia Variables (Ranch Hands Only)

Variable	ADJUSTED		
	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
Malignant Systemic Neoplasms (Testicles) (D)	NS	NS	NS
Malignant Systemic Neoplasms (Ill-Defined Sites) (D)	--	--	--
Malignant Systemic Neoplasms (Connective and Other Soft Tissues) (D)	--	--	--
Carcinomas in Situ of the Penis, Other, and Unspecified Sites (D)	--	--	--
Hodgkin's Disease (D)	ns	ns	ns
Leukemia (D)	--	--	--
Non-Hodgkin's Lymphoma (D)	ns	ns	ns
Other Malignant Neoplasms of Lymphoid and Histiocytic Tissue (D)	ns	ns	ns
Multiple Myeloma (D)	--	--	--
Skin or Systemic Neoplasms (D)	**(ns)	**(NS)	**(ns)
Laboratory			
Prostate-Specific Antigen (D: Below vs. At or Above Sensitivity Limit)	ns	NS	ns
Prostate-Specific Antigen (C: Measurements At or Above Sensitivity Limit)	ns	ns	ns
Prostate-Specific Antigen (D)	**(NS)	**(NS)	**(NS)

C: Continuous analysis.
D: Discrete analysis.
-: Relative risk < 1.00.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant ($p > 0.10$).
NS* or ns*: Marginally significant ($0.05 < p \leq 0.10$).
**(NS) or **(ns): Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.05$); not significant when interaction is deleted; refer to Appendix F-2 for further analysis of this interaction.
**(ns*): Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); marginally significant when interaction is deleted; refer to Appendix F-2 for further analysis of this interaction.
**(...): Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); significant when interaction is deleted and p-value given in parentheses; refer to Appendix F-2 for further analysis of this interaction.
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes a relative risk of 1.00 or greater; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

Table 10-49.
Summary of Group-by-Covariate and Dioxin-by-Covariate Interactions from Adjusted Analyses of Neoplasia Variables

Model	Variable	Covariate
1[a]	Prostate-Specific Antigen (C: Measurements at or Above Sensitivity Limit)	Insecticide Exposure
	Prostate-Specific Antigen (D)	Lifetime Cigarette Smoking History
2[b]	Malignant Skin Neoplasms	Insecticide Exposure
	Nonmelanoma	Insecticide Exposure
	Malignant Systemic Neoplasms	Lifetime Cigarette Smoking History
	Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck)	Lifetime Cigarette Smoking History
	Prostate-Specific Antigen (C: Measurements at or Above Sensitivity Limit)	Age
3[c]	Malignant Skin Neoplasms	Industrial Chemical Exposure, Insecticide Exposure
	Basal Cell Carcinomas (Trunk)	Insecticide Exposure
	Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck)	Lifetime Cigarette Smoking History, Degreasing Chemical Exposure
	Malignant Systemic Neoplasms (Prostate)	Degreasing Chemical Exposure
	Prostate-Specific Antigen (C: Measurements At or Above Sensitivity Limit)	Insecticide Exposure
	Prostate-Specific Antigen (D)	Insecticide Exposure
4[d]	Basal Cell Carcinomas (Trunk)	Insecticide Exposure
	Malignant Systemic Neoplasms	Degreasing Chemical Exposure
	Systemic Neoplasms of Uncertain Behavior or Unspecified Nature	Asbestos Exposure
	Malignant Systemic Neoplasms (Prostate)	Degreasing Chemical Exposure
	Skin or Systemic Neoplasms	Eye Color
	Prostate-Specific Antigen (D)	Degreasing Chemical Exposure
5[e]	Skin Neoplasms	Skin Color, Industrial Chemical Exposure
	Benign Skin Neoplasms	Skin Color
	Basal Cell Carcinomas (Trunk)	Insecticide Exposure
	Malignant Systemic Neoplasms	Lifetime Cigarette Smoking History, Degreasing Chemical Exposure
	Systemic Neoplasms of Uncertain Behavior or Unspecified Nature	Asbestos Exposure
	Malignant Systemic Neoplasms (Prostate)	Degreasing Chemical Exposure
	Skin or Systemic Neoplasms	Eye Color
	Prostate-Specific Antigen (D)	Degreasing Chemical Exposure

Table 10-49. (Continued)
Summary of Group-by-Covariate and Dioxin-by-Covariate Interactions from Adjusted Analyses of Neoplasia Variables

Model	Variable	Covariate
6[f]	Skin Neoplasms	Skin Color, Industrial Chemical Exposure
	Benign Skin Neoplasms	Skin Color
	Basal Cell Carcinomas (All Sites Combined)	Asbestos Exposure
	Basal Cell Carcinomas (Trunk)	Insecticide Exposure
	Malignant Systemic Neoplasms	Lifetime Cigarette Smoking History, Degreasing Chemical Exposure
	Systemic Neoplasms of Uncertain Behavior or Unspecified Nature	Asbestos Exposure
	Malignant Systemic Neoplasms (Prostate)	Degreasing Chemical Exposure
	Skin or Systemic Neoplasms	Eye Color
	Prostate-Specific Antigen (D)	Degreasing Chemical Exposure

C: Continuous analysis for measurements at or above the prostate specific antigen sensitivity limit.
D: Discrete analysis.
[a] Group Analysis (Ranch Hands vs. Comparison).
[b] Ranch Hands—Log_2 (Initial Dioxin).
[c] Categorized Dioxin.
[d] Ranch Hands—Log_2 (Current Lipid-Adjusted Dioxin + 1).
[e] Ranch Hands—Log_2 (Current Whole-Weight Dioxin + 1).
[f] Ranch Hands—Log_2 (Current Whole-Weight Dioxin + 1), Adjusted for Total Lipids.

relationship between initial dioxin and the neoplasia endpoint. Histories of neoplasia among Ranch Hands decreased as initial dioxin levels increased. Most of the significant resulting analyses, both unadjusted and adjusted, were among the skin neoplasia endpoints: skin neoplasms, malignant skin neoplasms, basal cell carcinomas (all sites combined), basal cell carcinomas (ear, face, head, and neck), nonmelanoma, and melanoma. Analysis of benign skin neoplasms and basal cell carcinomas of the upper extremities showed marginally negative significant results for both unadjusted and adjusted analyses.

Of the history of systemic neoplasia endpoints, malignant systemic neoplasms and malignant systemic neoplasms of the thyroid gland displayed significant negative unadjusted associations with initial dioxin. Adjusted malignant systemic neoplasms of the thyroid gland results were also significant. For all of these endpoints, the history of a neoplasm decreased as initial dioxin increased. The ability to detect significant differences for most of the site-specific systemic neoplasms was limited by the small number of participants with a history of a neoplasm at any given site.

The analyses of skin and systemic neoplasms revealed significant results for both the unadjusted and adjusted analyses. Prostate-specific antigen was significant in the unadjusted analysis for both the continuous and discrete versions. The discrete association was marginally significant in the adjusted analysis. As for the other endpoints, prostate-specific antigen decreased as initial dioxin increased.

Model 3: Categorized Dioxin Analysis

Similar to the Model 2 analyses, most significant results from Model 3 were among the skin neoplasia endpoints. Of all the significant skin neoplasia contrasts, most were the result of the low Ranch Hands versus Comparisons unadjusted contrasts from the analyses of skin neoplasms, malignant skin neoplasms, basal cell carcinoma (ear, face, head, and neck), and nonmelanoma. The unadjusted background Ranch Hands versus Comparisons contrast and the adjusted low Ranch Hands versus Comparisons contrast from the skin neoplasms analysis also were significant. The estimated relative risks were each greater than one, indicating a higher history of a skin neoplasm in Ranch Hands with background or low dioxin levels than in Comparisons; however, the estimated relative risks were marginally significantly less than one for Ranch Hands in the high category, indicating an inverse dose-response relationship. Contrasts of Ranch Hands versus Comparisons for benign skin neoplasms, basal cell carcinomas (all sites combined), and melanoma also displayed marginally significant estimated relative risks greater than one in either the background Ranch Hand category or the low Ranch Hand category versus Comparisons contrast. Again, the results were nonsignificant for the Ranch Hands in the high dioxin category.

Of the history of systemic neoplasia endpoints analyzed, any significant or marginally significant result again was from the low Ranch Hands versus Comparisons contrasts, and relative risks were greater than one. The results of the contrast of high Ranch Hands with Comparisons were not significant. The history of a malignant systemic neoplasm of the colon and rectum endpoint displayed significant differences for both the unadjusted and adjusted low Ranch Hands contrasts. Differences from the unadjusted analysis of any malignant systemic neoplasms also were significant and the adjusted results were marginally

significant. No significant results were seen in the high Ranch Hand category versus Comparisons contrast.

Other Model 3 results include another marginally significant low Ranch Hands versus Comparisons contrast as a result of the unadjusted analysis of a skin or systemic neoplasm. Also, the discrete prostate-specific antigen analysis revealed significant unadjusted and adjusted differences between background Ranch Hands and Comparisons, although more Comparisons than background Ranch Hands had abnormal prostate-specific antigen levels. The high Ranch Hands versus Comparisons contrast from the continuous prostate-specific antigen unadjusted analysis also was significant with higher prostate-specific antigen measurements in the Comparison group. The ability to detect significant differences for most of the site-specific systemic neoplasms was limited by the small number of participants with a history of a neoplasm at any given site.

Models 4, 5, and 6: Current Dioxin Analyses

Analyses of Models 4, 5, and 6 allowed examination of the relationships between neoplasia endpoints and different forms of current dioxin. Patterns found in Models 2 and 3 also were present in Models 4 through 6. Most significant and marginally significant results were found in the skin neoplasia endpoints, specifically: skin neoplasms, malignant skin neoplasms, benign skin neoplasms, basal cell carcinomas (all sites combined), basal cell carcinomas (ear, face, head, and neck), and nonmelanoma. All significant or marginally significant associations from analyses of Models 4 and 5 also were significant in Model 6. The Model 5 analyses revealed only marginally significant results for all the skin neoplasia endpoints listed above. The basal cell carcinomas of the ear, face, head, and neck adjusted analyses revealed marginally significant results in the Model 6 analysis, but nonsignificant in all other adjusted analyses. Each significant association was of an inverse nature, where disease among Ranch Hands decreased as current dioxin levels increased.

A history of malignant systemic neoplasms of the oral cavity, pharynx, and larynx was the only systemic neoplasia endpoint that displayed any statistical association with current dioxin, and the relationship was only marginally significant for Models 4, 5, and 6.

Unadjusted analysis of a history of a skin or systemic neoplasm revealed significant results for Model 6, and each continuous prostate-specific antigen unadjusted analysis was significant for Models 4, 5, and 6. The estimated relative risk for both variables was less than one, indicating a decrease in disease as dioxin levels increase. After covariate adjustment, however, each of the aforementioned analyses were nonsignificant. The ability to detect significant differences for most of the site-specific systemic neoplasms was limited by the small number of participants with a history of a neoplasm at any given site. However, there is excellent power to detect an increase in overall malignant disease.

CONCLUSION

Analyses of all Ranch Hands and Comparisons indicated no significant difference between the two groups. When analyzing associations between initial dioxin and neoplasm endpoints within the Ranch Hand group, Ranch Hands in the background dioxin category and

Ranch Hands in the low dioxin category tended to be higher than Comparisons, whereas Ranch Hands in the high category often were lower than Comparisons. Parallel to analyses using initial dioxin, results observed when current dioxin was used as the measure of exposure often indicated a negative dose-response relationship. In summary, there appears to be no clinical difference between Ranch Hands and Comparisons, and there is no evidence to suggest a positive dose-response relationship between dioxin and neoplastic disease.

CHAPTER 10
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